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**EPA'S ACTION CONCERNING
NITRILOTRIACETIC ACID (NTA)**

HEARING
BEFORE THE
**SUBCOMMITTEE ON
OVERSIGHT AND INVESTIGATIONS**
OF THE
**COMMITTEE ON
INTERSTATE AND FOREIGN COMMERCE**
HOUSE OF REPRESENTATIVES
NINETY-SIXTH CONGRESS
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EPA'S ACTION CONCERNING NITRILOTRIACETIC ACID (NTA)

THURSDAY, JUNE 26, 1980

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS,
COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE,
Washington, D.C.

The subcommittee met, pursuant to notice, at 9:30 a.m., in room 2359-A, Rayburn House Office Building, Hon. Bob Eckhardt (chairman) presiding.

Mr. ECKHARDT. I would like to call to order the hearing today on the Environmental Protection Agency's action concerning nitrilotriacetic acid, NTA, in laundry detergents.

After World War II, synthetic detergents largely replaced soap as cleansing aids for laundry, and phosphates became the major "detergent builder." Since that time, phosphates in domestic wastewater have become a principal contributor to the rapid process of eutrophication observed in many inland waters. Hence, there has been pressure to restrict the use of phosphates, and in that context NTA was developed as a substitute "detergent builder."

However, in 1970 studies at the National Institutes of Health suggested that NTA should be restricted and its use discontinued in the United States pending further review. Subsequently, the major manufacturers of NTA voluntarily withdrew this substance from the U.S. market.

During the intervening decade, many other nonphosphate substitutes have been marketed, including carbonates, silicates, and citrates. At the same time, research on the health and environmental effects of NTA has continued, and this research has established a carcinogenic effect on the urinary tract and kidneys of both rats and mice when exposed to high dietary levels of NTA.

With that as background, the Environmental Protection Agency, in response to a request from Procter & Gamble and Monsanto, conducted a risk assessment of NTA in laundry detergents. This risk assessment was completed on April 22, 1980, and the results of this assessment were communicated to Procter & Gamble in a letter of May 27, 1980 [see appendix, p. 299, this hearing]. In this letter, EPA concluded that the levels of exposure from the use of NTA in laundry detergents would be low, and the agency indicated that there would be no reason to take regulatory action against the resumed production and use of this substance in laundry detergents.

The hearing today will focus upon the issuance by EPA of this letter to Procter & Gamble. I believe that several significant issues relative to the implementation of the Toxic Substances Control Act,

TSCA, are posed by this EPA action. Within the policy objectives of TSCA, the use of NTA as a detergent builder presents important scientific and policy questions that need to be addressed.

For example, we are interested in pursuing why the agency risk assessment excluded the consideration of substitute detergent builders. We intend to probe whether substitutes, such as carbonates, present a safe and effective alternative to phosphates and NTA. We are also concerned that the voluntary environmental monitoring suggested by EPA in its letter of May 27 may not adequately insure the protection of the public health and environment. Thus, we will investigate whether more comprehensive environmental studies are necessary and whether such studies should be conducted under enforceable requirements if NTA is reintroduced.

The subcommittee will first receive information from Representative James Martin, our colleague from North Carolina. His testimony will be followed by a panel of distinguished scientists and a detergent and chemical industry panel. We will conclude with a presentation by EPA.

Mr. Lent, do you have an opening statement?

Mr. LENT. Thank you, Mr. Chairman.

Today's hearing will focus on a number of significant scientific and policy questions. Issues such as the introduction of chemicals into the environment and the procedures by which that is achieved will be aired.

Over recent years we have made quantum leaps in our knowledge of scientific matters. Because of our increasingly sophisticated knowledge, we are far more environmentally aware today than we were 10 years ago. Our testing procedures have become so exact we can detect minute amounts of toxic elements in most substances. Some chemicals considered harmless a short time ago are now recognized as potentially dangerous.

The increasing sophistication presents us with the problem of determining what is a level of acceptable risk. I believe careful, analytical risk assessments may provide us with a partial solution. A careful evaluation of risks helps us decide whether to permit the manufacture or use of certain substances.

That apparently is what EPA had attempted to do with NTA. I commend them for their efforts. After sifting through the realms of data available on NTA, EPA decided that projected levels of exposure from the use of this substance in laundry detergents are generally low and, therefore, that the associated risks would also be low. Obviously some doubt remains. All questions have not been answered.

In my opinion, no matter how much testing is performed on chemicals, doubts will always remain, questions will remain unanswered, and there will be room for debate and differences of opinion, but that is the nature of science. In order to avoid endless second-guessing about the risks of chemicals, someone must be vested with the authority to evaluate conflicting data and make decisions. EPA has been given that authority, and in this case it appears it exercised it in a careful and justifiable manner. I support the methodology used by EPA in reaching what is a difficult decision.

Mr. ECKHARDT. Mr. Maguire has been most interested in this area of concern and has been a leader in bringing this debate to consideration.

Mr. MAGUIRE. Thank you, Mr. Chairman.

At the outset, let me say to you that I am grateful to you for your leadership and willingness to devote the resources of the subcommittee to us this morning.

For the past 6 years our Interstate and Foreign Commerce Committee, and this subcommittee in particular, has been trying to come to grips with the fundamental proposition—that is, what constitutes an appropriate Federal cancer policy?

In the course of our many inquiries in this area we have identified and codified into law some basic practices and procedures to bring some organization to this extremely important national effort. We determined that good policy requires interagency and interdepartmental consultation among representatives from OSHA, NCI, EPA, and NIEHS, for example. Therefore, when an agency is contemplating the use of a toxic substance or carcinogen, the highest level and broadest range of expertise would be brought to bear on the decisionmaking process.

We determined that risk assessment studies, careful evaluations of scientific evidence, and peer review should prevail, so that decisions were made scientifically, in the open, with appropriate public comment and insulated from political pressure or industrial power. We wanted, in short, decisions on the merits.

We determined that a preventive approach, one in which we shied away from introducing even low-risk carcinogens into the biosphere, made the most sense in terms of the careful use of our health care dollars and as a regulatory strategy. I might add that our committee embodied this philosophy in the Biomedical Research Act Amendments of 1978.

We have more to learn about shaping the Federal response to cancer, but consultation, careful consideration of the best scientific evidence, and a reliance on prevention are three approaches which we have adopted and used successfully.

What concerns me about the case which we will be discussing this morning is that the Environmental Protection Agency's approval of the use of nitrilotriacetic acid, NTA, as a detergent additive ignores each of the basic precepts of our cancer policy. In fact, I would say that some of them were flaunted.

Mr. Chairman, we will learn this morning that none of the responsible Federal officials from the interagency cancer task force were consulted in an official capacity when the decision was made to permit the dumping of 1 billion pounds per year of NTA, a known carcinogen, into our Nation's water supply.

We will learn that the scientific methods used for extrapolating the human risk factor by the introduction of NTA into our waters has been challenged by several reputable authorities, more evidence that consultation was needed prior to the approval of the application.

In one of the more appalling aspects of this entire affair, we will learn that EPA, after contracting with Midwest Research Institute to perform a workable and consumer exposure assessment of NTA, permitted Procter & Gamble to see a draft of the assessment and

propose changes, some of which were accepted, which changed the tone and character of the report.

The changes which will be shown to the committee will demonstrate that Procter & Gamble wanted the report to show that the possibility of harm from the use of NTA was less likely than was actually the case as determined by the contractor.

Mr. Chairman, your willingness and desire to become involved in this issue is appreciated. It is my hope that the subcommittee will diligently pursue this investigation and think hard about how we can apply this lesson of true regulatory lapse to help make our cancer prevention strategy a proven and effective one.

Thank you, Mr. Chairman.

Mr. ECKHARDT. We have at this time our distinguished colleague, Representative James G. Martin, as our first witness here.

We have an invariable rule of swearing our witnesses at our hearings, Representative Martin.

Do you swear to tell the truth, the whole truth, and nothing but the truth, so help you God?

Mr. MARTIN. I will swear to do the best I can to tell the truth, the whole truth, and nothing but the truth, Mr. Chairman.

Mr. ECKHARDT. You may proceed.

TESTIMONY OF HON. JAMES G. MARTIN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NORTH CAROLINA

Mr. MARTIN. Mr. Chairman, the hearing which you and members of the committee had set for today is very timely, raising yet another landmark question of public policy before this committee, and I want to commend you for your initiative.

The Environmental Protection Agency has announced its approval of nitrilotriacetate, NTA, for use as a substitute for sodium polyphosphate as a detergent builder. It is expected that NTA will now be used in detergents only in those areas like the Great Lakes region where phosphate has been a major contributor to eutrophication. The question you are asked to consider is whether scientific evidence of toxicity, carcinogenicity, and teratogenicity warrant a ban on NTA.

The related, but overriding issue, in my judgment, is whether the new policy that EPA has evolved for evaluating such risks is good public policy. I contend that it is; I welcome the balanced relative risk assessment approach which EPA has developed, in contrast to the zero risk mentality that pervades the Occupational Safety and Health Administration; and I urge you to commend this approach of EPA rather than drive them back to the nonscientific nonsense of the absolute zero risk advocates.

Now you know which side I'm on. I am sure it must be viewed with puzzled exhilaration at EPA to have so far consistent Republican support on this particular matter.

Let me amplify the perspective that I have for the fledgling philosophy that is to me so welcome at EPA, and for which their leadership should be encouraged, not thwarted.

Back in 1976 and 1977 B.S.—that is, "before saccharin"—the absolute zero risk standard, enshrined in the Delaney amendment to the food safety laws, pervaded the ranks of EPA consultants as they proposed a new regulation, since withdrawn, to remove car-

cinogens from the environment—at least the industrial chemicals if not the natural ones.

The narrow scientific orthodoxy used to support that early EPA proposal came under serious attack from a group of highly regarded toxicologists. One of them, Dr. Philippe Shubick and his Eppley Research Institute in Omaha, Nebr., have had to pay the price for successfully challenging that orthodoxy, for a series of General Accounting Office and Inspector General's Office investigators have been delegated to harass him and intimidate him and interrupt his career and send a chilling message to others who might dissent from this absolute safety fetish. This raises problems for the Congress in obtaining independent scientific witnesses.

As another historical footnote, those same environmental defense activists who lost their bid to extend the Delaney amendment to EPA have since transferred over to more fertile ground at the Occupational Safety and Health Administration, where that old regulatory chemophobia has been reincarnated.

Since 1978, EPA has evolved in the direction supported by the vast majority of American scientists, namely, the more rational approach endorsed by a continuing series of consensus statements from the learned scientific societies, including the National Academy of Sciences, which sets relative risk assessment instead of the obsolete absolute as a basis for carcinogen regulation.

Instead of banning every known carcinogen, no matter how remote the risk, EPA has championed in this administration the idea of considering the evidence of relative potency and the actual exposures encountered by consumers, workers, whatever, in determining whether a risk has a high probability or a very low probability or in between, and matching the enforcement program, if warranted, to the degree of risk. That is just what EPA has done in ruling on NTA.

I hope this committee will agree that this is a far more rational approach to public policy in dealing with exposure to chemicals found to cause cancer. In this present case, EPA has estimated that any residual risk to humans from the traces of NTA not biologically degraded is a significantly smaller risk than what we considered with saccharin. You will recall we have already bombed that ban. The EPA estimate for NTA is a risk on the order of 1 in 2 million lifetimes; that is, less than one a year in the whole population of the Great Lakes region.

If you feel that risk is too great and that we should ban all risks of this magnitude, most of the universe itself will be set off limits. To even plaster warning labels like the one on saccharin on all products posing such a low risk will only paper over the marketplace with a continuum of ubiquitous cancer scares. They will receive no more attention from the consequently jaded public than does the saccharin warning label. That would be a tragedy, Mr. Chairman, because there are, after all, some real wolves out there, and we'd best not distract people about the relative puppies.

Others will deal with the specific scientific issues. I urge you not to overlook this fundamental question of public policy in dealing with science. I urge you not to thwart EPA in its new approach of relative risk assessment, but rather to encourage them and other agencies to continue this kind of balanced approach favored by the

consensus of American scientists and generally accepted as the basis for chemical regulation in all other civilized nations.

That concludes my statement, Mr. Chairman. I thank you for the opportunity to be here.

Mr. ECKHARDT. Thank you for a very good and witty statement.

Mr. MARTIN. It was written late last night, Mr. Chairman, which often happens.

Mr. LENT. I want to express my appreciation to our colleague, Jim Martin, for his views this morning. I would like to ask him if he would be interested in elaborating on his views on relative risk assessment. For example, would you tell us what steps you think Congress might take to see that the agencies charged make increased use of relative risk assessments in their regulatory decisionmaking?

Mr. MARTIN. Yes. I thank the gentleman from New York for that question. As a matter of fact, I have drafted legislation dealing with food safety law amendments to amend not only the Delaney clause but the general safety provisions as well, to propose and to provide for a consideration of relative risk assessment. We would take into account not only which substances are shown by various scientific evidence to be carcinogens, but also take into account how potent that evidence indicates the substance to be. Further, take into account, as I said a moment ago, the probable exposure to the public and higher risk subgroups of the public in determining what the probability of risk will be to those people so exposed.

I think we should also take into account the benefits. Very often the benefits are in the nature of risks avoided by the use of a substance. The units are not always the same. They cannot be precisely balanced, but at least benefits ought to be considered, not ignored.

In the particular framework that we are facing today we have a recent decision by an interagency regulatory group, including EPA, OSHA, the Consumer Products Safety Commission, FDA, and others, which has led to an Executive order signed by the President of the United States which does call for consideration of risk assessment in determining the appropriate policy for regulating chemical exposures in the field of carcinogenicity. I think we should encourage that rather than try to discourage it, thwart it, back them off into the kind of policies that seemed more reasonable two decades ago.

Mr. LENT. As I understand it, in the subject matter we are discussing today, the EPA's decision vis-a-vis NTA, we have a situation where the NTA was perhaps the subject of the most thorough chemical analysis in history. It was the subject of a study by the HEW. There was an international joint commission task force on NTA, which involved Canadian experts and others. There were some 20 years of exhaustive testing by industry and other governments involving NTA, including Sweden, Finland, Canada, and the Netherlands, all of which have approved NTA for use in detergents, as I understand it.

After analyzing these studies this material was given a clean bill of health by EPA for use in detergents. We are now conducting oversight of EPA to see if what they did was the right thing, if

their procedure was correct, and if they came to the right conclusion.

Do you feel that we ought to encourage EPA to continue testing materials in the manner which they have tested the NTA?

Mr. MARTIN. Certainly, Mr. Lent. That is the gist of my statement that I made, and that is the philosophy which I have.

I certainly recognize that, human nature being what it is, such as allegations that are already being made, there are going to be examples where someone may have erred along the way. That is unfortunately one of the general aspects of human nature, as I mentioned. Nevertheless, it is the best scientific effort we can make, the best scientific effort that is possible for humans on this planet.

I think we should encourage that kind of approach which bases its judgment on relative risk assessment rather than on an absolute zero risk policy, which only creates fear of chemicals without differentiating which ones are most potent and which ones are least potent in these effects. I think we should encourage that. I would hope that would be the outcome of these hearings—that it would reassure the members that it is the best kind of scientific analysis we can get and encourage other agencies to do likewise, hopefully leading toward a rewrite of the food safety laws in this same kind of direction that I have advocated and many of the members of this committee have advocated for the past 3 years.

Mr. LENT. I have no further questions, Mr. Chairman. I appreciate the views of our colleague, who is perhaps the outstanding Member of Congress in the field of chemistry.

Mr. ECKHARDT. Mr. Maguire?

Mr. MAGUIRE. Thank you, Mr. Chairman.

Mr. Martin, you have been a leading advocate of cost-benefit analysis. I wonder if you have examined the benefit side of this equation. For example, have you made an assessment of NTA versus carbonates as a detergent builder?

Mr. MARTIN. No, sir. I have reviewed the discussion in the available literature which deals with the question of benefits, the replacement of polyphosphate. I do not pose to be an expert on whether or not there may be some alternative ingredient available, if that is the purpose of the gentleman's question.

I am generally aware of that argument, but the statement that I made has resided primarily on the kind of approach taken by the Environmental Protection Agency in considering essentially the relative risk and also taking into account benefits.

Mr. MAGUIRE. A risk-benefit analysis would presumably need to involve more careful analysis than that of the benefit side of the equation, would it not?

Mr. MARTIN. Do you mean by me?

Mr. MAGUIRE. By whomever.

Mr. MARTIN. By the Environmental Protection Agency. I would not quarrel with their approach to considering the benefits.

Mr. MAGUIRE. Are you aware that they have not, in fact, examined the question of the benefit side with respect to NTA versus alternative detergent builder compounds, such as carbonate?

Mr. MARTIN. No, I am not aware of that. I am not sure of what significance it would be, but the gentleman is quite right that I

have not examined all the flaws of what they neglected to look at. They probably did not look at cyanide. They probably did not look at a number of others.

Mr. MAGUIRE. You have applauded EPA in your statement. I wonder if you agree with EPA that NTA should not be used in detergents designed for hand dishwashing, for shampoos, and for food.

Mr. MARTIN. I think there is a reasonable exercise of prudence on the part of the Environmental Protection Agency in making a distinction for the direct use of nitrilotriacetate. You will notice that what they have argued is that a considerable amount of the material that gets into the lakes, streams, and water supply which is then biologically degraded, leaving very small traces—detectable but very small estimated amounts—to which the general public would be exposed. It is on that basis, as I understand it, that they have estimated an extremely low level of residual risk.

Mr. MAGUIRE. But they have recommended that NTA not be used in situations where human hands and other parts of the body would be directly exposed to the chemical.

Mr. MARTIN. I am aware of that. I have no objection to that.

Mr. MAGUIRE. You would endorse that?

Mr. MARTIN. I have no objection to that whatsoever. They have to make a judgment as to what the relative risk is. It is also probable that NTA will not be used in areas where phosphate is still permitted, because of the lesser cost of the phosphate.

Mr. MAGUIRE. I think that is an interesting question. Perhaps we can explore that with the witnesses later.

Would you agree that people who buy laundry detergents might in fact use those detergents for the handwashing of clothes or even handwashing of dishes?

Mr. MARTIN. That is certainly possible.

Mr. MAGUIRE. Would you recommend that a warning label be placed on the detergent in view of the fact that EPA has recommended that it not be used in that fashion?

Mr. MARTIN. I would say to my colleague that it has been my general approach on warning labels that we should reserve those warning labels for cases which involve the greatest care, for cases which involve significant risks. If the Environmental Protection Agency in its estimate believes that there would be significant exposure from that, I would welcome their recommendation accordingly.

We have already put such a warning label on saccharin, which, as the gentleman knows, is a far more fearsome warning label than the one that is on a package of high-tar, high nicotine cigarettes manufactured in my State.

Mr. MAGUIRE. Perhaps the gentleman can work with me to strengthen the warning on cigarettes.

Mr. MARTIN. Or perhaps to delete the warning from saccharin, because it merely confuses people and creates a general blasé attitude about warning labels. We have to be very careful about that.

If there is a determination that that potential exposure is such that people should be careful not to drink the stuff or eat it as they work with it or wash their hands in it, I have no objection to

advising them of that on the package. They probably will not read it.

Mr. MAGUIRE. You are aware that at least at some levels of exposure laboratory animals do get cancer from NTA?

Mr. MARTIN. Yes, sir.

Mr. MAGUIRE. It is, therefore, a carcinogen in the way that term is ordinarily used by the scientific community?

Mr. MARTIN. I am prepared to accept that argument. As to whether it is an initiator or promoter, of course that would be subject to further debate. You will probably hear some discussion of the quality and interpretation of that evidence that you have cited. You are also probably going to hear some question of evidence that relates to the possibility that you may be overwhelming various kidney, blood, or other functions of the animal. These are things that have to be taken into account by you as well as the Environmental Protection Agency.

I am satisfied that the Environmental Protection Agency has considered these questions and has come to its own conclusion that the evidence, as you have referred to it, is valid, but that it poses a very remote risk in the normal use—the residual risk in the normal use—of such products.

Mr. MAGUIRE. Have you had an opportunity to examine the question of where as a scientist you would establish the threshold in a relative risk assessment process with respect to this compound?

Mr. MARTIN. When you are speaking of threshold, you are not talking in the sense of threshold of the effect with increasing dose. You are talking about a policy or a regulatory action level threshold. Am I correct?

Mr. MAGUIRE. I am talking about the threshold below which you might argue that cancer would not be produced in human beings as a result of average exposures.

Mr. MARTIN. No, I would not rest a case on an argument about a threshold below which there would be no effect whatsoever. I would rest the case on the basis that the Environmental Protection Agency has—that even if you assume there is an effect based on the high dose evidence, even if you assume that predicts an effect in humans at very low doses, after the biodegradation that would ensue the residual effect is going to be so small that it is on an order of magnitude that should not cause great concern. It is well within a range of low cancer risks which we ordinarily and without too much concern take everyday.

I tried to be responsive to the gentleman's question. I would not rest this case on the question of an effect threshold.

Mr. MAGUIRE. I can certainly understand how, if health and life were involved in both sides of the equation, one would want to look very, very carefully at both the benefit side and the risk side with respect to an individual compound. I am wondering how many additional cases of cancer in the population you would find acceptable in exchange for people being able to perhaps get somewhat whiter washes in some parts of the country where there may be harder water or phosphates cannot be used.

Mr. MARTIN. Let me thank the gentleman for the very gentle way in which he has expressed the age-old bugaboo about how

many cancer deaths are you in favor of. I think he has been very polite and courteous in his restatement of that old terrorist question.

Yes, I am prepared to make such a decision. I think the policy-making body of this Government, the Congress, is going to have to eventually make such decisions. It would seem to me that we would make them on the basis of a comparison of this risk in question with other risks which we are aware of and which can be measured and estimated based on actuarial totals and so forth, and which relate to similar practices which are perhaps cosmetic in nature and which have a cancer death risk on about the same level.

Mr. MAGUIRE. However, if I could show you that you could get clothes white with carbonates, why would you accept any level of risk at all for the introduction of NTA?

Mr. MARTIN. My overriding philosophy on this, Mr. Maguire, is somewhat different. That is that if the risk is so extremely remote that it is well within a range of risk that people willingly take in an otherwise free society every day, I see no point in the Government stepping in to deny them a choice of how they are going to proceed when the risk is so exceptionally small. I would let people make some of those decisions on their own.

Mr. MAGUIRE. You use the phrases "extremely remote" and "exceptionally small." Not even EPA uses those words in its analysis. It tends to use the word "low," which is not quite in the same category.

We will hear from a panel of scientific witnesses. Perhaps we can further clarify this.

Thank you, Mr. Chairman.

Mr. MOFFETT [presiding]. Are there questions from the gentleman from Pennsylvania?

Mr. MARKS. First, I would like to mention that we have a full committee markup. I have an amendment coming up this morning. Therefore, I possibly will not be back.

We appreciate very much having our colleague here with us this morning.

Mr. MARTIN. Thank you, sir.

Mr. MARKS. I have only one question, if I may. Would you recommend any changes—you talked around this—in the Toxic Substances Control Act which would more clearly direct EPA to utilize what we call the risk assessment in the future?

Mr. MARTIN. I would certainly support that. It would be somewhat redundant at the moment, inasmuch as that is their intention to proceed in that way with the present leadership of the Environmental Protection Agency. That is a philosophic concept which has been, with their leadership and that of the Consumer Products Safety Commission and a couple others, presented very persuasively to the President. He has acted upon it with an Executive order.

However, looking toward the future when there could be changes in all of these levels of authority, it might be well to reinforce that with suitable legislation. Yes, I would certainly support that. I would support it in relation to other agencies, such as OSHA, which are reluctant to consider relative risk assessment. Their approach is that a substance is a carcinogen or it has not yet been

shown to be one and, therefore, they make no distinction between relative potency or relative degree of risk. I think that is a mistake on their part.

Mr. MOFFETT. The gentleman from California, Mr. Dannemeyer, is recognized.

Mr. DANNEMEYER. Mr. Maguire is not here. However, in light of his questions, Mr. Martin, I would like to know when you stopped beating your wife?

Mr. MARTIN. About an hour and a half ago.

Mr. MOFFETT. The gentleman from New York is recognized.

Mr. LENT. I wanted to ask one final question. I realize we have a vote in progress on the floor.

I just want to ask Mr. Martin what his opinion is of the risk of the use of phosphates as a builder in detergents as opposed to the use of NTA as a builder in detergents. I understand some States, such as New Jersey, still use phosphates.

Mr. MARTIN. Yes, and the States around the Great Lakes, in efforts to try to clean up the damage that has been done to the Great Lakes by overloading them with nutrient and with phosphate, most of it coming from fertilizer runoff rather than from detergent—nevertheless, in an effort to clean up that problem and try to revitalize in a sense those important bodies of water, they have required an abatement of the use of phosphates.

The benefit involved there is the restoration of the health of those lakes. That is an important consideration.

Mr. LENT. Thank you.

Mr. MOFFETT. The subcommittee thanks the gentleman from North Carolina for his testimony.

We are not going to recess even though members may want to go to this vote on the floor. Instead we will call our first panel:

Dr. Anne Spacie, assistant professor of fisheries and limnology, department of forestry and natural resources, Purdue University; Dr. Roger Perry, head of the public health and water resource section, Imperial College, University of London; Dr. Myra Karstadt, assistant professor of environmental medicine, Environmental Sciences Laboratory, Mt. Sinai School of Medicine; and Dr. David P. Rall, Director, National Institute of Health Sciences.

Please come forward.

As I think all of you know, it is the practice of the subcommittee to swear all witnesses. Would you please remain standing and raise your right hands?

Do you swear to tell the whole truth and nothing but the truth, so help you God?

Dr. SPACIE. I do.

Dr. PERRY. I do.

Dr. KARSTADT. I do.

Dr. RALL. I do.

Mr. MOFFETT. Thank you very much. Please be seated.

Let's have this batting order: Dr. Spacie, Dr. Perry, Dr. Karstadt, and Dr. Rall.

Before we begin your testimony, if each of you could state your full name, title, and affiliation for the benefit of the reporter and the record, we would appreciate that, beginning with Dr. Spacie, please.

Dr. SPACIE. Thank you. My name is Anne Spacie. I am an assistant professor of fisheries and limnology at the Department of Forestry and Natural Resources, Purdue University.

Dr. PERRY. I am Dr. Roger Perry of the Imperial College, London. I am head of the environmental engineering program.

Dr. KARSTADT. I am Dr. Myra Karstadt. I am assistant professor of environmental medicine in the Environmental Sciences Laboratory, Mount Sinai School of Medicine, New York City.

Dr. RALL. Thank you. I am Dr. David Rall, Director of the National Institute of Environmental Health Sciences, U.S. Public Health Service.

Mr. MOFFETT. Dr. Spacie, as I said, we would like you to begin.

I would say this to each of you: We know you do have prepared statements. Without objection, those statements will become part of the record. You may, of course, read those statements. We would hope that your testimony would run at about 10 minutes or under in the interest of time.

Dr. Spacie, please proceed.

TESTIMONY OF DR. ANNE SPACIE, MEMBER, TASK FORCE ON ECOLOGICAL EFFECTS ON NONPHOSPHATE DETERGENT BUILDERS, GREAT LAKES SCIENCE ADVISORY BOARD; DR. ROGER PERRY, HEAD OF PUBLIC HEALTH (ENVIRONMENTAL) AND WATER RESOURCE ENGINEERING, IMPERIAL COLLEGE, LONDON UNIVERSITY, UNITED KINGDOM; DR. MYRA KARSTADT, ASSISTANT PROFESSOR OF ENVIRONMENTAL MEDICINE, ENVIRONMENTAL SCIENCES LABORATORY, MOUNT SINAI, SCHOOL OF MEDICINE, NEW YORK CITY; AND DR. DAVID P. RALL, DIRECTOR, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES, NATIONAL INSTITUTES OF HEALTH, PUBLIC HEALTH SERVICE, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Dr. SPACIE. Thank you.

I am here today as a member of the Great Lakes Science Advisory Board's task force on ecological effects of nonphosphate detergent builders. The Great Lakes Science Advisory Board advises the International Joint Commission on technical issues concerning the Great Lakes under the 1978 Great Lakes Water Quality Agreement between Canada and the United States.

The IJC has recognized the role of phosphorus in lake eutrophication and has called for the reduction of phosphorus sources, including phosphate-based detergents. Because this restriction would lead to the substitution of alternative builders, the science advisory board created a task force in 1977 to investigate the potential ecological effects of such nonphosphate builders. The task force, chaired by Joseph Shapiro, examined available information on currently used and proposed builders to report on their ecological acceptability.

The task force issued a report on NTA in 1978. A second report on other organic builders—citrate, carboxymethyltartronate, and carboxymethyloxysuccinate—has been completed and is now under review by the science advisory board. A third report on inorganic builders—carbonate, silicate, and zeolites—is in preparation.

These reports evaluate each builder in terms of chemistry, degradation in wastewater and the environment, contribution to eutrophication, and possible biological effects. My contribution to the task force has been in the area of aquatic toxicology.

I would first like to review some of the findings of the task force on NTA and to give you its recommendations for further study of this builder. The task force concludes that the use of NTA does not constitute an obvious environmental hazard. However, a number of important questions about the behavior of NTA remain. These concerns are essentially identical to those raised in the U.S. Environmental Protection Agency's risk assessment document on NTA. Based on a review of available information, the task force recommends that NTA should not be prohibited from use as a detergent builder. The task force further recommends that the use of NTA be accompanied by studies to address several areas of concern. I will list those.

First, NTA ordinarily degrades rapidly and completely in aerobic waste treatment systems and in most freshwater environments. However, Canadian monitoring programs have found low concentrations of NTA in receiving waters. An increase in builder NTA content in Canada also resulted in higher concentrations in wastewater discharged to the environment. The task force feels that the reason for NTA remaining in the environment should be investigated.

Second, the ability of NTA to degrade during anaerobic waste treatment or under anaerobic environmental conditions is questionable. Rates of degradation in flooded soils, groundwater, and anaerobic lake water are apparently slower than they are under aerobic conditions. The task force feels that the question of anaerobic degradation needs further study.

Third, no investigations have been conducted to determine the concentrations of NTA in anaerobically digested sludges. Such sludges are frequently deposited in landfills or at sea, where remaining NTA might become available to plants or animals.

Fourth, little, if any, information is available on the removal of NTA by physical-chemical treatment processes such as alum or lime coagulation, carbon adsorption, et cetera.

Fifth, NTA degradation has been studied at intermediate pH values but not under more extreme conditions such as those found in acidified lakes and streams—pH below about 5.

Sixth, degradation of NTA in marine and estuarine environments appears to be very slow. In estuarine systems there apparently is inhibition of the degradation performed by freshwater organisms. Further study on this inhibition is required.

Seventh, NTA does not solubilize and transport heavy metals to an appreciable extent under most circumstances. However, it has been shown to increase the transport of metals through waste treatment systems under certain conditions. The task force feels that its behavior in systems of high inorganic turbidity or high metal content, such as those in mining operations, needs investigation.

Eighth, available information indicates that acute or chronic toxicity to aquatic organisms resulting from environmental concentrations of NTA is unlikely. However, the mode of toxic action has

not been well defined. Without this information, it is difficult to predict the chronic effect of NTA under a variety of conditions. Several reports also raise questions concerning the ability of NTA to produce lesions in marine organisms. These studies should be reviewed and extended.

Ninth, NTA is not expected to increase the eutrophication of lakes by providing nutrients from its decomposition. Most experiments with simple systems indicate that it does not stimulate algal growth. However, long-term studies using whole ecosystems have not been performed to the extent of proving that NTA will not cause significant changes in the aquatic community structure.

One of the least satisfying aspects of the testing of detergent builders has been that of the effects on aquatic communities. Too often studies have been done using single species, and when community studies were done they were either unrealistic, too short, insufficiently studied, or omitted important aspects of the community.

The monitoring programs in Canada have been designed to measure the presence or absence of NTA in water. They have not addressed the question of environmental effects in any direct way. If NTA is to be used on a large scale in the United States, studies designed to measure biological effects in a variety of environments are essential.

The task force has examined a number of builders that may serve as alternatives to NTA. Three such builders—citrate, carbonate, and silicate—are naturally occurring and are expected to have little, if any, effect on the environment at the concentrations expected in wastewater. All three of these are currently used to some extent as substitutes for phosphate. Two other organic compounds are currently under consideration as possible builders. These are carboxymethyloxysuccinate—CMOS—and carboxymethyltartrate—CMT.

The task force concluded that CMOS is not likely to be detrimental to the environment. However, there are several concerns about its behavior in waste treatment systems and its ability to complex metals in natural waters that require further study.

The use of the builder CMT is not endorsed by the task force at this time because CMT appears to degrade more slowly in aerobic and anaerobic waste treatment systems than do the other organic builders.

The use of zeolite builders is currently under review by the task force, and no recommendations are available at this time.

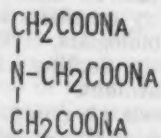
For your reference, I have appended a chart showing the structures of the organic builders so that you can compare the properties of each one.

Mr. MOFFETT. Thank you very much, Doctor, for your very interesting statement. That chart will be made part of the hearing record.

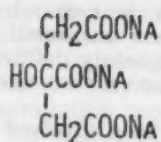
[The chart referred to follows:]

ORGANIC DETERGENT BUILDERS

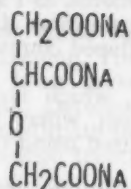
SODIUM NITRILOTRIACETATE (NTA)



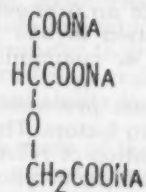
SODIUM CITRATE



SODIUM CARBOXYMETHYLOXYSUCCINATE (CMOS)



SODIUM CARBOXYMETHYL TARTRONATE (CMT)



Dr. Perry, please proceed.

TESTIMONY OF DR. ROGER PERRY

Dr. PERRY. Mr. Chairman, I have been asked to appear before you because a considerable amount of research work dealing with the environmental effects of nitrilotriacetate has been carried out by the Public Health and Water Resource Engineering Section of Imperial College, which is under my supervision. This section is comprised of 8 faculty members and 50 graduate students, including chemists, microbiologists, civil and chemical engineers, pursuing a research program dealing with many aspects of water quality and waste water treatment.

As head of this research group, I have visited many parts of the world, frequently under the auspices of the World Health Organization or the British Council. I have noted over the years the increasing trend toward water reuse, and in this context I am concerned about the possible wider implications of the recent EPA decision relating to NTA.

I believe, based upon the research in which I have been involved, that there are problems associated with the use of this material that have been inadequately defined in the literature, and there are other areas of concern that need detailed scientific investigation.

Clearly, I have not been involved with the health-effects side of NTA, but rather have devoted my research effort to a study of NTA as it affects metal mobilization in wastewater treatment plants and how its biodegradation or lack thereof is of concern with current wastewater and sludge treatment processes.

Aspects of these problems, as I see them, are briefly:

First, regarding wastewater treatment, sewage treatment as practiced in most developed countries involves three major processes:

One, sedimentation, which is a removal of the coarse solids;

Two, aerobic oxidation, where the organic materials in solution or suspension are oxidized using trickling filters or activated sludge processes; and

Three, disposal of the sludge obtained primarily from No. 1 above and partly from No. 2 above, usually following anaerobic digestion.

In each of these processes the use of NTA in detergents could have far-reaching adverse effects, and I contend that many of these effects have been inadequately studied and in other cases data presented have been of an over-generalistic nature, being applicable to a unique situation in one area of the world which is not relatable to an area or community relying heavily upon water reuse.

In biological oxidation processes, Imperial College has been involved in a study of two factors. These are:

First, the biodegradation of NTA in the activated sludge process, and, second, the possible occurrence of heavy metal transfer to the receiving waters caused by the presence of NTA.

This work has clearly shown that although NTA biodegrades under ideal conditions, where the sewage treatment work has a constant hydraulic load and influent NTA concentration and a high temperature, under realistic conditions of wastewater treat-

ment, where there is a variable hydraulic load, a variable influent NTA concentration and fluctuating temperatures, significant changes in the degree of biodegradation take place. These are accompanied by mobilization of heavy metals from the sludge into the effluent.

Both laboratory scale and pilot plant studies utilizing realistic levels of NTA and heavy metals have demonstrated these facts. This presents a very different picture to that which has been published relating to the Canadian experience.

The situation in Canada, as I see it, is briefly as follows:

With an average NTA content in detergents of 15 percent, this gives rise to an NTA concentration of about four parts per million in sewage treatment works influents. Corresponding average effluent NTA concentrations are about 0.6 ppm. After dilution in the receiving waters, surface water NTA concentrations reported for Canada average about 0.003 part per million or three parts per billion (ppb).

If the same level of NTA were introduced in Western European detergents and a similar average degree of biodegradation were assumed, I would anticipate the following:

Influent concentrations of NTA in sewage would be 15 ppm, representing the different degree of water use. Effluent concentration, assuming the same biodegradation took place, would be 2.4 ppm. After typical dilution of 8-to-1, this would result in 300 ppb NTA in the receiving waters.

If it is assumed that the same range of variations occur, namely, a tenfold variation, in Europe as occurs in Canada, this could give rise to 3,000 ppb as a maximum level. The consequences of such a situation have not been evaluated.

I would like to emphasize that these figures are realistic in relation to the River Thames in London. The data that have been used in these calculations have been taken from our Standing Technical Committee on Synthetic Detergents publications. The dilution factors, if anything, underestimate the situation.

Next, I would like to address sludge treatment and disposal. In view of the recent emphasis on energy conservation and the requirement to dispose of increasing quantities of sewage sludge to land, a study has been initiated at Imperial College to examine the biodegradation of NTA under conditions of anaerobic sludge treatment. Apart from consideration of the possible nonbiodegradability of NTA itself, concern was felt about changes in heavy metal availability which this would cause and which would subsequently be reflected in crop uptake and transfer to groundwater. Currently, guidelines for sludge disposal are being evaluated by many countries and the concept of metal availability is receiving a great deal of attention.

To my knowledge, no detailed study of the degradation of NTA under these conditions has been undertaken, and in my opinion it is essential that this information be made available. Preliminary indications from our own work at Imperial College would suggest problems in anaerobic degradation of NTA under sewage treatment conditions.

My conclusions, therefore, Mr. Chairman are that:

One, data on NTA concentrations in surface waters in geographical areas where high effluent dilutions take place cannot be related to those from areas where low effluent dilutions occur and where water reuse is practiced. In this situation more data are required concerning the variable biodegradation of NTA, particularly as influenced by temperature, heavy metal concentrations, and sewage treatment plant operating conditions.

Two, metal mobilization has been shown to occur under conditions of variable NTA influent loading. An assessment needs to be made of this factor with respect to current water quality standards.

Three, it is considered that NTA degradation under anaerobic conditions is severely limited and that this will have significant repercussions in sludge disposal to land. These factors need rigorous scientific investigation, particularly from the standpoint of metal availability.

Four, very little is known about the biodegradability of NTA in sea water, and this again needs detailed evaluation from the standpoint of both sewage discharge and sludge disposal.

Finally, I believe that the influence of United States practice in relation to activities in developing countries should again be considered, particularly where arid communities are utilizing settled sewage and effluents directly for irrigation purposes.

Thank you.

Mr. MOFFETT. Thank you very much, Dr. Perry.

Dr. Karstadt, please proceed.

TESTIMONY OF DR. MYRA KARSTADT

Dr. KARSTADT. Mr. Chairman, Mr. Lent, ladies and gentlemen, thank you for inviting me to testify on NTA. I have submitted a rather lengthy statement for inclusion in the record. I will summarize that statement very briefly this morning.

Mr. MOFFETT. Your prepared statement in its entirety will be made part of the hearing record [see p. 21].

Dr. KARSTADT. On May 27, 1980, Steven Jellinek, Assistant Administrator of EPA for Pesticides and Toxic Substances, sent a letter to Procter & Gamble which in effect cleared the way for use by Procter & Gamble of NTA as a detergent builder in the United States.

In the EPA document which serves as the backup for the May 27 letter, "Final Report: NTA," which I will henceforth refer to as FRN, EPA sets out many unresolved questions about potential and environmental effects of NTA use. These questions may be serious and include the possibility of dissemination of a potential environmental carcinogen.

NTA has been shown to cause urinary tract cancer in rodents. EPA estimates human risk of urinary tract cancer of drinking water exposure to NTA to be "low," approximately 1 in 500,000. This estimate of risk is based on a quantitative risk assessment which uses animal bioassay data and data obtained from monitoring of Canadian drinking water for NTA.

The use of quantitative risk assessment for direct extrapolation of bioassay data from animals to man is controversial in the scientific community. Because of the informal manner in which EPA handled decisionmaking on NTA, the scientific community has not

had an opportunity for full and open discussions of the use of quantitative risk assessment for NTA or the execution of the risk assessment itself.

EPA assumes that 1 in 500,000 is a "socially acceptable" risk, not meriting application of EPA's regulatory resources. This assumption deserves extensive public discussion.

EPA also raises many questions about possible effects of NTA on the environment. Perhaps the most immediately important question is whether NTA stimulates or inhibits algal growth. The rationale for using NTA is that it will not contribute to eutrophication and algal overgrowth in the Nation's waters, but EPA notes that there is a conflict in the scientific literature as to whether this is indeed the case.

Possible eutrophic effects of NTA should be resolved as soon as possible because a chemical about which there may be any reservations as to potential adverse effects on human health should also not have other effects disadvantageous to the public.

EPA notes that there are other significant questions about NTA's effects on plants and animals of the aquatic environments into which the chemical will be released. NTA is assumed to break down well in the waters into which it is discharged and, therefore, it is assumed that environmental and human exposure to NTA will be low. However, EPA raises many questions in the FRN regarding biodegradation of NTA, pointing out conditions in which NTA does not biodegrade well or conditions which require further study.

There is also evidence from Canadian monitoring studies of a low-level persistent concentration of NTA. This persistence is evidently not fully understood.

With all the uncertainties about the breakdown of NTA in water, EPA relies for estimates of U.S. exposure on Canadian drinking water monitoring data. In FRN, EPA raises what may be serious questions about the Canadian data, pointing out methodological flaws in the Canadian studies.

Even if the Canadian data are valid for Canada, EPA points out factors which might render the Canadian data of questionable validity for the United States. Among other things, compared to Canada the United States has increased per capita use of detergents, increased population density, and therefore increased NTA load per unit of stream into which NTA is discharged, and differing climatic and geographic conditions.

Given the differences between the United States and Canada and the unknown factors surrounding breakdown of NTA, it may be difficult to establish an average exposure level for drinking water in the United States with confidence. Many separate levels may be needed to reflect differing conditions and unknown factors. If it is not possible to set an exposure estimate in which there is great confidence, then the quantitative risk assessment is open to doubt.

With all these uncertainties about NTA, it seems reasonable that EPA use the Toxic Substances Control Act—TSCA—to require that manufacturers and/or detergent formulators perform tests to resolve the unanswered questions about NTA before the chemical is marketed as a detergent builder in the United States. However, EPA has not used TSCA in regard to NTA and has not required any testing.

Mr. Eckhardt, the chairman of this subcommittee, and Mr. Broyhill, ex officio member of the subcommittee, in cooperation with Mr. Staggers, the chairman of the full committee, devoted a great deal of time and effort to insure that the Toxic Substances Control Act would afford EPA opportunities for collecting information on chemicals and for reasonable and well-reasoned regulation of toxic substances.

EPA should use TSCA as it was intended in the case of NTA applying section 5 of the act to insure that this chemical will not pose an "unreasonable risk of harm to health or the environment," to use the language of the act.

NTA was already in use in the United States at the time TSCA became effective, January 1, 1977, but use of NTA as a detergent builder would constitute "a significant new use" of an existing chemical as discussed in section 5(a) of the act.

In order to require that testing of NTA be carried on before the chemical is used on a large-scale basis as a detergent builder, section 5(e), "Regulation Pending Development of Information," should be invoked by EPA.

It would be advantageous if testing and monitoring, and perhaps development of exposure estimates for the United States, were to be required by EPA.

In summary, a rulemaking might well be initiated immediately by EPA under section 5 of TSCA to have use of NTA as a builder in laundry detergents designated a significant new use of NTA, and to require that unresolved questions regarding possible adverse effects of NTA on health and the environment be resolved before the chemical is put into use as a detergent builder in the United States.

Thank you very much.

[Testimony resumes on p. 30.]

[Dr. Karstadt's prepared statement follows:]

STATEMENT OF MYRA KARSTADT

BEFORE THE

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

HOUSE INTERSTATE AND FOREIGN COMMERCE COMMITTEE

June 26, 1980

My name is Myra Karstedt. I am Assistant Professor of Environmental Medicine and a member of the staff of the Environmental Sciences Laboratory at the Mount Sinai School of Medicine, New York City. I received a Ph.D. in Biophysics (Nucleic Acid Biochemistry) from the University of California, Berkeley, in 1969 and a J.D. from Harvard Law School in 1972. My research and teaching interests include the science, law and policy issues involved in regulation of toxic substances.

In the EPA publication, "Final Report:NTA", (April 22, 1980) many questions remain unresolved about potential health and environmental effects of NTA. These questions are serious and include the significant possibility of dissemination of a potential environmental carcinogen. The unresolved questions should be answered by EPA's requiring testing of NTA before it is put into use as a detergent component in this country.

Background Information

According to the "Final Report:NTA" (henceforth, FRN), the current production volume for NTA in the United States is approximately 70-75 million pounds per year, of which approximately 10-15 million pounds are used in this country. The remaining production is exported for use in detergents in Canada and Europe. EPA estimates that if NTA is used in heavy duty laundry detergents in the United States, as much as 1.1 billion pounds of NTA could be used in this country in 1982 (Table 2, p. 7). Also, the FRN notes that "if NTA is used widely in the United States detergents, virtually the entire population will be exposed through drinking water contaminated with NTA derived from wastewaters, and through the use of consumer products containing NTA...Based on the limited data available, it is expected the typical exposure via these routes will be low." (FRN, p. 21).

Potential Carcinogenicity of NTA

NTA has been shown to cause urinary tract cancer in rodents. EPA, in its FRN using estimated exposures based on monitoring data from Canada and results of NCI bioassays of Na₂NTA has calculated the risk to the general population exposed to NTA in drinking water at approximately 1 in 500,000, a level reported as "quite low". (FRN, p. 45)

The Task Force on the Health Implications of NTA (a report to the Grand Lakes Research Advisory Board of the International Joint Commission, 1977), used Canadian monitoring data and animal bioassay results to estimate the risk of urinary tract cancer in rodents. Average drinking water exposure to NTA in Canada was estimated at 0.07ug/kg/day. The risk of urinary tract cancer in rodents exposed to that level of NTA was estimated as less than 2×10^{-7} (Reported in Subcommittee Report: Review of Proctor and Gamble Statement Regarding Carcinogenesis of NTA for Executive Committee of National Toxicology Program, undated (early 1980), p. 21. Risks for workers in detergent formulation plants who also have drinking water and consumer product exposure to NTA are estimated at 1 in 4,000, but the report notes that the worker population is small and the exposures could be lowered if dust masks were worn. (FRN, p. 45).

Proctor and Gamble has proposed mechanisms for NTA carcinogenesis which would imply a threshold dose for the compound. The Proctor and Gamble data were considered by the subcommittee of the National Toxicology Program (whose report is cited above), which concluded, after examining the data presented by Proctor and Gamble: "...we do not know the mechanism of NTA carcinogenesis and do not know what level of exposure constitutes a threshold, if there is a threshold." (Subcommittee report: Review of Proctor and Gamble, etc., above; p. 2).

In his letter of May 27, 1980, to Mr. W. C. Krumrei, Senior Director, Research and Development, of Proctor and Gamble Company, Steven Jellinek, Asst. Administrator of EPA for Pesticides and Toxic Substances, states: "Our review... finds that the projected levels of exposure from the use of

(NTA) in laundry detergents are generally low and therefore that the associated risks would also be low. Based on these findings and on the higher priority demands upon our limited resources, EPA sees no reason to take regulatory action against the resumed production and use of this substance for laundry detergents."

Important questions of regulatory policy are raised on this unusual EPA action regarding non-regulation of NTA. First, it is assumed that one can make a simple quantitative extrapolation from limited data obtained in animal studies to human cancer risk. Such a "guesstimate" is offered by EPA; it would seem essential that the agency set out the scientific rationale for the process used in arriving at the estimated risk, especially since there is wide uncertainty in the scientific community about the use of quantitative risk assessment. Second, an assumption is offered that this risk of 1 in 500,000 is "socially acceptable". According to the New York Times, Robert Coyer, Deputy Director of NIEHS: "said that the scientific evidence did suggest that the risks from NTA were lower than those from many other carcinogens. But he added that science and the Government had not yet determined whether any level of risk from a cancer-causing agent was "acceptable".

"He also suggested that society had not yet really addressed the question of whether it really wanted exposure to even a weak carcinogen in return for a commercial value such as a better detergent, adding, "we still do not have the tools to make such a judgment". (Shabecoff, Philip, Chemical Is Cleared For Detergent Use, The New York Times, June 11, 1980, p. 20.)

On the question of carcinogenicity alone, the NTA action by EPA raises important questions which merit discussion with other agencies involved in regulation of toxic substances and which merit discussion within the scientific community and by the public. For instance, is any level of risk from a cancer-causing agent "socially acceptable" if the risk can be identified and avoided? EPA evidently failed to discuss its actions or the implications of its actions with sister regulatory and research agencies. The public was not included in the decision-making, and groups which have previously expressed interest in water pollution (Environmental Defense Fund, Natural Resources Defense Council) and relevant Congressional committees were not informed of the action during the process of decision-making or after the decision was made. This hearing is really the first chance for a public airing of the questions made explicit or implied in EPA's actions regarding NTA.

Potential Environmental Impact of Use of NTA Eutrophication

But carcinogenicity is only one potential adverse effect of NTA. In the FRN, EPA raises many questions about possible effects of NTA on the environment. Perhaps the most immediately important question, requiring an answer as soon as possible, is whether NTA stimulates or inhibits algal growth. The rationale for using NTA as a substitute for phosphate is that NTA should not contribute to "eutrophication" of waters into which it is discharged. "Eutrophication", a process in which certain nutrients in bodies of water exist in over-supply, results in overgrowth of algae. It is noted on p. 62 of FRN that: "The results of studies with algae can perhaps be summarized best by Prakash, (1976) who pointed out that studies on the effect of NTA on metabolism and growth of planktonic algae in freshwater and the marine environment have been anything but consistent, demonstrating both growth inhibition or growth stimulation, depending upon the

species tested and the water characteristics. The available literature indicates that NTA might affect algae growth by three major routes: 1) by perhaps supplementing direct nitrogen requirements of phytoplankton upon degradation, especially in nitrogen limited waters (i.e., estuaries, coastal water and oligotrophic lakes)....."

On p. 64 of FRN, the discussion of possible eutrophic effects of NTA is concluded by noting that NTA will not pose a major risk of serving to increase algal growth. These calculations are based on Canadian monitoring data for NTA in wastewaters, and assume low levels of N introduced into the aquatic environment by degradation of NTA.

The IJC Task Force notes that: (Appendix FRN IJC Task Force, Recommendation' 9)

"NTA is not expected to increase eutrophication by providing nutrients from its decomposition. Furthermore, most experiments with simple systems indicate that it does not stimulate algal growth. However, the long term studies using whole ecosystems have not been performed to the extent of satisfying the Task Force that NTA will not cause significant changes in aquatic community structure. Such experiments are necessary.

"One of the least satisfying aspects of the testing of detergent builders has been that on the aquatic community. Too often studies have been done using single species of algae, and when community studies were done they were either unrealistic, too short, insufficiently studied, or omitted important aspects of the community. Studies of the results to date do not raise any specters, but the final answer is not yet in."

The levels of risk of harm from intact NTA are calculated as low for man and the environment because of assumptions that NTA will break down satisfactorily in the United States waters, (for EPA's reservations on this subject, see below). However, if NTA does break down, N will be released to the waters, and the possibility of eutrophication will exist. Possible eutrophic effects of NTA should be resolved as soon as possible, because the benefits of a chemical about which there may be any reservations as to potential adverse effects on human health, should also not have other effects disadvantageous to the public.

Possible Adverse Effects on Aquatic Organisms

EPA notes that there are other significant questions about NTA's effects on the plants and animals of the aquatic environments into which the chemical will be released. For instance, in the FRN, EPA reports on an experiment on a marine teleost fish in which chronic exposure to levels of NTA which could occur near wastewater discharges caused intestinal lesions. Although the experiment was reported in the literature in 1972, it has evidently not yet been repeated to determine its significance. According to EPA (p. 60): "Eisler concluded that NTA might present a significant hazard to marine teleosts and higher invertebrates when used as a partial replacement for sodium tripolyphosphate in household detergents." This experiment should be repeated on several species of fish to determine its validity and general applicability.

EPA also notes that "Canadian monitoring has only attempted to determine the presence (or absence) of NTA, and has not investigated effects or impacts, such as possible subtle shifts in algal populations or productivity. Detailed environmental monitoring for such effects is appropriate." (FRN

p. 64). On p. 65 of FRN, EPA states that: "NTA's possible effects on saltwater algae and its effects on other estuarine organisms, such as the shell forming mollusks, should be investigated. Also desirable are additional studies involving chronic exposure of mixed communities to low levels of NTA to determine NTA's possible effects on behavior, physiology, histopathology and cytopathology of aquatic organisms."

NTA is evidently not a mutagen or teratogen. It is not acutely toxic to animals except at high levels of intake. Questions do remain unanswered about low-level chronic effects of intact NTA and about the possible eutrophic effects of the breakdown products, particularly N, of the detergent builder.

Biodegradation of NTA

NTA is assumed to break down well in the waters into which it is discharged and therefore exposure to NTA is assumed to be low. However, EPA raises many questions about the biodegradation of NTA. The assumption of low exposure is called into question.

The FRN (p. 12) states: "There is considerable evidence from both laboratory studies and field observations that NTA, even when complexed with metals, biodegrades substantially and rapidly in aerobic, non-saline waters... Before optimum degradation can occur, the bacterial population must be acclimated to NTA for a period of two weeks or more. Other requirements include moderately high ambient temperatures (greater than about 5°C) and low NTA loadings." NTA evidently does not biodegrade well at low temperatures. In fact, biodegradation approaches zero in "un-aerated lagoons" in sewage treatment plants at temperatures below 5°C (FRN, p. 12, 14). There are also unresolved questions about NTA breakdown at high temperatures, the temperatures found in thermophilic waste treatment processes (FRN, Appendix, Summary of Report of International Joint Commission Task Force on the Ecological Effects of Non-phosphate Detergent Builders-NTA 1978, Joseph Shapiro, Chairman, recommendation 5).

The special climatological conditions of the American South also merit consideration. On p. 19 of FRN, EPA states that: "In view of the slower degradation of NTA under anaerobic and micro aerobic conditions and in consideration of the fact that oxygen is less soluble in warm water than in cold water, it may be that a potential for high NTA concentrations in United States waters would exist in warm waters with high organic loadings, such as in southern swamps and in highly polluted streams at summer temperatures, (which conditions often coincide with low stream flows and consequent reduced dilution). This is a possibility which will have to be carefully watched if NTA is introduced into the United States detergent market."

NTA degrades best in non-saline water. EPA reports that NTA appears to break down slowly in marine environments, but it evidently does not biodegrade in estuarine environments.

EPA notes that: "The question of NTA degradation in saline waters needs to be more fully understood, especially before any significant ocean dumping of sewage sludges which may contain undegraded NTA is allowed." (FRN, p. 15).

According to EPA (p. 12): "Relatively little is known about the degra-

dation of NTA under anaerobic conditions...if significant concentrations of NTA should accumulate in the environment, it is most likely that this will happen in areas of low oxygen concentration, particularly if the temperature also is low."

pH also may play a factor in NTA degradation, and this area demands further study. The International Joint Commission noted that NTA biodegradation has been studied between pH5 and pH9, and with increased acidity of lakes in the Northeastern United States because of the so-called "acid rain", data are needed on breakdown of NTA at pH below 5. At the other end of the pH scale, the IJC notes that "Many eutrophic softwater lakes, particularly those requiring wastewater effluents, maintain pH values well in excess of 9 for long periods of time." (FRN Appendix, IJC Task Force on the Ecological Effects of Non-phosphate Detergent Builders-NTA 1978-Joseph Sharro, Chairman, recommendation 3).

NTA behavior in various forms of sewage treatment plants also needs further study. Thus, the International Joint Commission notes that: "Although NTA does degrade in aerobic waste treatment, the Task Force feels that its behavior in physical-chemical treatment processes needs elucidation."

"Little if any information is available on the removal of NTA by such processes as alum coagulation, lime coagulation, iron coagulation, carbon absorption, etc. Although such processes are likely to follow aerobic wastewater treatment, their effects on NTA should be known." (FRN Appendix, IJC Task Force above, recommendation 4).

Anaerobic degradation of NTA may be especially important for study because of possible dumping of anaerobically-digested sludges in the ocean or on land. The IJC notes that: "No investigations have been conducted to determine the concentrations of NTA in anaerobically digested sludges. Canadian studies have shown that about one-third of the NTA appears to be lost from solution during primary treatment. Because it may be settled out in the sludge and because sludge is frequently deposited in the sea and on land, investigation is necessary." (FRN Appendix, IJC Task Force above, recommendation 3).

Questions are also open regarding NTA's solubilization of metals and breakdown of NTA-metal chelate complexes. (FRN Appendix, IJC Task Force above, recommendation 7, FRN p. 19, p. 16).

There is evidence from Canadian water monitoring statistics, of a "relatively persistent background level of a few ug/l" of NTA "possibly due to the complexation of NTA as the more persistent chelates with Cu, Zn, or Ni". (FRN, p. 18). The IJC Task Force (FRN Appendix, IJC Task Force, above recommendation 1) notes that: "... from the Canadian experience, NTA does appear to persist at low levels and it is important to know whether this is because of the kinetics of microbial activity, or because of the presence of non-degradable chelates..."

Finally, on p. 19 of FRN, EPA makes several recommendations for studies on breakdown of NTA. Aspects which should be studied include: possible increase in the concentration of metals in sewage sludges; NTA degradation in natural anaerobic environments; degradation in saline water, particularly differing degrees of breakdown in marine and estuarine environments; per-

sistent low levels of NTA; levels of NTA in anaerobically-digested sludges; environmental fate of NTA at pH below pH5 or below pH9. EPA, regarding these unresolved questions, states that: "There are a number of uncertainties with respect to the fate of NTA on the environmental research should be conducted to resolve as many of these uncertainties as possible..." (FRN, p. 19).

Exposure Estimates

With all these questions remaining open as to breakdown of NTA in water, EPA, for its estimates of exposure in the United States, relies heavily on Canadian monitoring data. On p. 18, p. 222 and p. 60 of FRN, EPA raises what may be serious questions about the validity of the Canadian monitoring data, noting flaws in program design and "differences in analytical methods, uncertainties about sample preparation, and a lack of replicate sampling." (FRN, p. 18). On the other hand, data relied on were taken during the coldest months, and are therefore assumed to be "worst-case" estimates (FRN, p. 21). According to EPA: "Nevertheless, there seems to be little reason to doubt the overall conclusions from the Canadian monitoring experience..." (FRN, p. 18). However, there is quite a difference between accepting the overall qualitative conclusions of the Canadian data—that NTA does seem to break down under some conditions (see above) and that "a relatively persistent background level of a few ug/l may be found, possibly due to the complexation of NTA as the more persistent chelates with Co, Zn, or Ni" (FRN, p. 18) and use of specific numbers from the Canadian studies for calculation of human risk of cancer in the United States.

Even if the Canadian exposure data are valid for Canada, EPA, in its FRN, points out factors which might render the Canadian data of questionable validity for the United States. Compared to Canada, the United States has: increased per capita detergent use, increased population density (therefore increased load/unit of stream into which NTA is dumped), and differing climatic and geographic conditions (FRN, p. 23 et alia).

Given the differences between the United States and Canada and the unknown factors surrounding breakdown of NTA, it is difficult to establish an "average" exposure level for drinking water in the United States with confidence. Many separate levels may be needed to reflect differing conditions and unknown factors. If it is not possible to set an exposure estimate in which there is great confidence, then the quantitative risk assessment is open to doubt.

EPA Should Use Section 5 of TSCA to Require Testing of NTA to Resolve Unanswered Questions Before The Chemical Is Used In Detergents In The United States.

With uncertainties outstanding about possible effects of NTA on human health and the environment, and with the need for data on actual levels of NTA in water and breakdown of NTA during its residence in various aquatic environments, it seems reasonable that EPA require that manufacturers or detergent formulators perform tests and monitoring of NTA. This has not been done, however. In its letter to Proctor and Gamble, EPA suggested that Proctor and Gamble carry on monitoring and environmental studies (not specified) and give EPA an opportunity "to review the design of such studies."

The Toxic Substances Control Act was enacted in order to both obtain information on and regulate chemicals. In the case of NTA, EPA certainly needs information on a chemical which may be used in a manner so as to expose

virtually the entire population and the broad scope of the nation's waters.

NTA was already in production in this country at the time TSCA went into effect (January 1, 1977) and is, for TSCA purposes, defined as an "existing chemical"; that is, NTA appears on the TSCA initial inventory.

Section 5 of TSCA provides that information must be submitted to EPA on two classes of chemicals before the chemicals are marketed. One class is comprised of "new" chemicals; that is, chemicals which do not appear on the TSCA initial inventory because they were not in production in the United States during the time period set out in the inventory regulations. The other class, into which NTA falls, is existing chemicals to be manufactured for a "significant new use". For these two classes of chemicals Section 5 requires that pre-manufacture (or processing) notification be submitted to EPA at least 90 days before the manufacture or processing is to begin. Certain basic data must be submitted on the chemicals, (Section 5 (d)(1)) and a notice of receipt of the pre-manufacture notification is to be published in the Federal Register (Section 5 (d)(2)). The Federal Register notice is the means through which the public obtains access to participation in regulatory decision-making regarding new chemicals or existing chemicals subjected to a significant new use.

It would appear that NTA to be used in laundry detergents in the United States, should be regulated under Section 5 as a "significant new use". Of an existing chemical NTA fits the criteria to be considered in rule-making for a "significant new use" in Section 5 (a)(2)). The projected volume of production and processing for use in detergents in the United States will be both very large and much increased from the current production volume.

Use of NTA in heavy-duty laundry detergents will change the type of exposure of both humans and the environment, since this use is new. If there is some use in laundry detergents in the United States at this time, "use as a builder in some minor brands of United States detergents (industrial source)" (FRN, p. 5), that use is so minor in volume (included in a group of "miscellaneous uses" with a total production volume of 0.8 million lbs.), the current use is minimal compared to the possible 1.1 billion lb. use contemplated, and the planned use of large volumes of NTA in detergents would still constitute a "new use". The contemplated high-volume use of NTA would cause a very significant increase in the magnitude of human and environmental exposure to NTA, and once NTA is in our water, exposure will be constant, for all practical purposes. In fact, even if NTA use were discontinued after some time, the persistence of NTA evident in Canadian waters would ensure that NTA would remain in United States waters for some unknown time after cessation of use. (No data were given in FRN on the turn-over time of NTA in water or sediment; perhaps data on persistence after cessation of use are available from Japan, where, according to the "sub-committee reports: review of Proctor and Gamble statement" cited above, NTA was "previously used" in Japan before "manufacturers' withdrawal" (p. 22).

As to the extent to which the proposed use will increase the magnitude and duration of exposure, EPA notes in its FRN that: "If NTA is used widely in United States detergents, virtually the entire population will be exposed through drinking water contaminated with NTA derived from wastewater". The number of people exposed will increase greatly from the number assumed to be exposed at present, and certainly the level of NTA to which "virtually" all

Americans will be exposed will increase significantly due to the vastly increased production, use and discharge into water.

The anticipated methods of use and disposal will result in wide-spread dissemination of NTA in United States waters.

In summary, a rule-making should be initiated immediately under Section 5 to have use of NTA as a builder in heavy-duty laundry detergents, as contemplated by Proctor and Gamble and possibly other detergent manufacturers, designated a "significant new use" of NTA.

In order to open to public discussion the question of standards for "significant new use", EPA could have published a generic rule. Although TSCA has been in effect since January 1, 1977, EPA still has not published such regulations. The NTA situation is, therefore, the first opportunity for issues concerning "significant new use" to receive public review. Publication in the Federal Register of a proposed Section 5 regulation of NTA, would have alerted the public to this first known example of "significant new use" since the effective date of the Act.

In order to require that testing of NTA be carried on before the chemical is used on a large-sale basis as a detergent builder, Section 5 (e) should be invoked, following the procedures outlined in the Act. NTA meets the criteria for imposition of Section 5(e): Data available are insufficient for determination of effects on human health and the environment; manufacture, use, or disposal of NTA without such data "may present an unreasonable risk of injury to health or the environment"; since NTA will be produced for use as a detergent builder in very substantial quantities, NTA will enter the aquatic environment, and there will be wide-spread significant human exposure to NTA.

Coordination With Other Agencies

Finally, given the important policy questions raised regarding regulation of "low-risk" carcinogens, it would appear useful that EPA coordinate its actions with other regulatory agencies. Coordination of regulatory activities regarding toxic substances is one of the goals of TSCA, and the "Coordination" sub-section of Section 9 sets out Congress' interest in having TSCA administered with a minimally duplicative manner. The Inter-agency Regulatory Liaison Group, of which EPA is a member, has drafted several documents on cancer policy, and actions like those on NTA require consideration for their consistency with recommendations of the IRLG.

Mr. MOFFETT. Thank you, Doctor.
Dr. Rall?

TESTIMONY OF DR. DAVID P. RALL

Dr. RALL. Thank you, Mr. Chairman and members of the committee. I am very pleased to be here this morning to discuss health aspects of NTA.

I might parenthetically add that I have been at my present job since 1971, and one of the first problems I faced when I joined NIEHS was the controversy on NTA.

Since these are not my fields, I shall not deal with biodegradation, exposure levels, and ecological effects of NTA, but deal strictly with health effects.

I would like to submit the full statement for the record and very briefly summarize the critical points.

Mr. MOFFETT. Your prepared statement in its entirety will be made part of the hearing record [see p. 31].

Dr. RALL. In the statement I have included a fairly long and detailed history of the scientific information developed on the health effects of NTA and the various reviews and their conclusions. Let me simply quote the latest review and conclusion from the national toxicology program a few months ago:

"It is concluded that there is no evidence that NTA is a mutagen."

Two, "NTA is a renal urinary tract carcinogen in rodents."

Finally, "we do not know the mechanism of NTA carcinogenesis. We do not know what level of exposure would constitute the threshold if indeed there is a threshold."

I would like to conclude this brief statement by pointing out, even though we in the national toxicology program have predicted that NTA is a low risk carcinogen, as a science agency we simply cannot take the next step—that is, we cannot determine for the public that this low risk is an acceptable risk. This is a public policy decision. It goes beyond our role and expertise as a provider of scientific information.

That information we can provide may and should be used as one of the cornerstones on which public policy decisions are made, but it is only a cornerstone and not an entire foundation.

Thank you very much.

[Testimony resumes on p. 39].

[Dr. Rall's prepared statement follows:]



DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF
ENVIRONMENTAL HEALTH SCIENCES
P.O. BOX 12233
RESEARCH TRIANGLE PARK, N.C. 27709

STATEMENT OF

DR. DAVID P. RALL

DIRECTOR, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

BEFORE THE

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE

UNITED STATES HOUSE OF REPRESENTATIVES

JUNE 26, 1980

Thank you, Mr. Chairman and Members of the Committee:

I am pleased to be here today to discuss the toxicity of NTA. Let me begin by reviewing the history of NTA and our research on it.

In the late 1960's, public concern was increasing over eutrophication or aging of the nation's lakes. There was particular concern regarding Lake Erie, which had experienced an explosive growth of algae that deprived the water of much of its oxygen. Phosphates in laundry detergents were accused of contributing to this process and, by 1969, the use of phosphates in detergents had become an issue of national debate and controversy. By early 1970, with Federal, State, and local governments introducing legislation to ban phosphates in detergents, detergent manufacturers sought a suitable substitute.

Research and development and the screening of possible existing substitutes pointed to the chemical nitrilotriacetic acid, or NTA, as one of the best available products. NTA was inexpensive and already was in production by two firms. In addition, NTA appeared to be effective as a builder in detergents. Early in 1970, the detergent makers began substituting small amounts of NTA for phosphates. NTA was not viewed as a total substitute for phosphates; but its use would reduce the phosphate content.

Throughout 1970, while the detergent manufacturers were replacing part of the phosphates in their detergents with NTA, there was some concern over the question of NTA's possible health hazards. This concern was based on the fact that NTA, which is an active chelating or metal-binding agent, had not been studied adequately in terms of its

effects on heavy metal uptake and distribution in plants, animals, and particularly humans.

The first warning that NTA might cause problems on its own came when it was recognized that the chemical properties of this strong chelating agent could serve as the basis for potential hazards from excessive NTA concentrations in water supplies. At the May 1970 hearings of the Senate Public Works Committee, a report was submitted stating that NTA would not significantly reduce pollution and might even be a health hazard in some cases. More research was urged on the chelating properties of NTA before wide substitution of it was made.

At this point, the National Institute of Environmental Health Sciences (NIEHS) became involved. We undertook an animal study to determine if any toxic or adverse health effects were possible with the use of NTA. Our study found that the chelating property of NTA caused it to combine with heavy metals such as methylmercury and cadmium. We were concerned that this might enhance the risk of birth defects or teratogenicity resulting from simultaneous exposure to methylmercury or cadmium and NTA.

When the NIEHS study was presented to the Surgeon General, he decided that the Public Health Service should recommend a cautious approach to adopting NTA.

The Surgeon General and the EPA Administrator called representatives of the detergent makers to Washington, D.C., on December 17, 1970. After they heard the concerns of NIEHS and the Surgeon General's

suggestion that the use of the additive be discontinued, the manufacturers agreed voluntarily to hold NTA off the market in the United States.

A joint HEW-EPA statement to the public said that there was no evidence, at that time, to indicate anyone had been or was being harmed by the combination of NTA with metals in the environment. But, "prudence dictates not permitting a situation to develop in which harm may occur to man from the effects of the projected uses of NTA." Thus, the evaluation of NTA was to continue.

Subsequently, other countries, including Canada, began to market detergents with NTA; and detergent manufacturers conducted their own research to determine how harmful NTA was. Extensive testing was conducted throughout 1971; and our Department was asked to review these test results.

In September 1971, the Surgeon General, the EPA, and the Council on Environmental Quality (CEQ) jointly announced their conclusions regarding what was known about the health and environmental problems associated with NTA and with detergents in general. Although the concern that NTA might increase the teratogenic activity of the toxic heavy metals was not confirmed, new concerns had arisen regarding the carcinogenic potential of NTA. The National Cancer Institute (NCI) had reviewed the data of an NTA study sponsored by Proctor and Gamble which suggested, but did not prove, that NTA at high doses was carcinogenic and might damage the kidney. The Surgeon General, EPA, and CEQ recommended that NTA not be

used at that time because of the unresolved questions concerning its possible long-term effects on health and the environment. They said that the health hazards of the increasing use of other highly caustic substitutes for phosphates in laundry detergents also was cause for serious concern. EPA announced that it would try to identify those bodies of water in the country that had potential or actual eutrophication problems due to phosphates, and that it would assist the State and local governments in reducing the phosphates to the extent necessary through the treatment of municipal wastes. The government was trying to find a way to achieve two important goals: protecting the health of the American people, and improving the quality of the natural environment.

In 1972, the Assistant Secretary's Ad Hoc Group on NTA, after reviewing all available data on NTA, stated that the toxicity evaluation indicated that NTA is a reasonably safe compound under acute or short-term exposure conditions. Long-term, low-level exposure hazards to human health could not be evaluated from the available experimental data.

In 1974, HEW established a subcommittee of its Committee to Coordinate Toxicology and Related Programs (CCTRP) to review: (1) the Proctor and Gamble sponsored chronic feeding study, which suggested a possible cancer or carcinogenic risk; (2) an NIEHS study designed to look at the chronic renal toxicity of NTA, which indicated that renal adenomas occur; and (3) preliminary studies conducted through the NCI carcinogen bioassay program, which indicated a carcinogenic effect of

NTA treatment on the urinary tract in both mice and rats. The CCTRP subcommittee concluded that the available evidence was indicative of a carcinogenic effect of NTA.

Subsequently, several reviews, including one by the United States-Canadian International Joint Commission (IJC) in 1977, found that NTA caused no genetic defects and that, while it did cause cancer in test animals, risks for humans were low. During 1977, NCI released its carcinogen bioassay results, which showed that animals given large doses of NTA developed malignant renal tumors. Proctor and Gamble was continuing its own research on NTA and, eventually, was to ask the government to review all the scientific evidence again and, this time, to issue a risk assessment.

Our Department's National Toxicology Program (NTP) was asked to look at the evidence submitted by Proctor and Gamble which claimed to indicate that NTA is a secondary carcinogen. If NTA is a secondary carcinogen, this implies that a primary effect must be elicited before the secondary one can be. In the case of NTA, one part of the issue argues that crystallization of NTA salt in the bladder, which leads to stone formation, is the precursor (or primary effect) of bladder carcinogenesis (the secondary effect). Thus, prevention of crystallization would be expected to prevent bladder cancer induction. EPA also was asked to review the evidence that only minuscule amounts of NTA would ever be present in drinking water.

In January 1980, a subcommittee of the NTP concluded, after reviewing the literature and Proctor and Gamble data, that: (1) NTA is a

renal urinary tract carcinogen in rodents; (2) there is no evidence that NTA is a mutagen; and (3) the validity of Proctor and Gamble's claim that NTA acts as a secondary carcinogen has not been proved; thus, the mechanism of NTA carcinogenesis and the level of exposure that constitutes a threshold, if there is a threshold, are not known. Based on the animal data and the available evidence on NTA levels that persist in Canadian drinking waters where NTA use is permitted, the NTP subcommittee also stated that the excess risk to ^{rodents} ~~man~~ for developing urinary tract tumors if NTA is used is less than one in five million for lifetime exposure.

To summarize the scientific data, in 1974 the HEW CCTRP subcommittee concluded that the NIEHS study of NTA in drinking water indicated NTA had a carcinogenic effect on the urinary tract of rats used in the test. A later bioassay conducted by NCI confirmed these results. The US-Canadian IJC report in 1977 concluded: (1) the available data do not indicate NTA is either a teratogen or a mutagen; (2) the only evidence that might cause concern regarding the public health is the NIEHS and NCI studies, which showed cancer of the urinary tract in rats and mice; and (3) at levels of NTA to which humans are exposed in drinking water, the highest lifetime probability of tumor formation in rodents is within an order of magnitude of 1 in 2 million. In 1978, a task force of this commission recommended, because of concern over certain gaps in knowledge of the environmental effects of NTA, that studies should be conducted to address specific questions if the use of NTA is resumed in the United

States. In January of 1980 the National Toxicology Program stated, among other conclusions, that the level, if any, which constitutes an exposure threshold is not known. The scientific issue that still confronts us is whether or not NTA acts as a secondary carcinogen.

Proctor and Gamble (P&G) asserts that a dose level has been determined at which crystallization of NTA salt can be demonstrated in urine and, tentatively, in bladder. Below this dose level or concentration, crystallization is not observed. Thus, to prevent the secondary effect, the dose levels of NTA must be below the concentration at which crystallization is shown. P&G estimated that the dose to which humans will be exposed through the use of NTA is 300,000 times lower than the dose at which crystallization of NTA salt has been observed. But this theory (which appears reasonable), as well as the theory that the occurrence of kidney tumors is a secondary effect, must be proved. A scientific demonstration of the validity of these theoretical mechanisms must be pursued.

In concluding, even though we, through the National Toxicology Program, have predicted that NTA is a low-risk carcinogen, as a science agency we cannot take that next step. That is, we cannot determine for the public that this low-risk is an "acceptable" risk. That is a public policy decision; and it goes beyond our role and expertise as a provider of scientific information. The scientific information we can provide may be used as one of the cornerstones on which public policy decisions are made, but it is only a cornerstone, not the entire foundation.

Mr. MOFFETT. Thank you, Dr. Rall. Thank you all for very excellent testimony.

At this time the Chair will recognize members for questions. The Chair now recognizes the gentleman from New York, Mr. Lent.

Mr. LENT. Thank you, Mr. Chairman.

I would like to ask Dr. Karstadt one question concerning her testimony that TSCA should have been used here instead of the risk assessment that EPA utilized.

EPA's testimony of Dr. Jellinek a little bit later on, reviewing it in advance, addresses this point. He says, "Although our review was not conducted under the formal authority of a TSCA significant new use rule, it was in effect the functional equivalent of such an exercise. The main difference is that under the formal statutory scheme we would have had only 90 days to complete our review"—that would be under TSCA—rather than the nearly 2 years we took to conduct a thorough evaluation."

In view of that statement, do you still feel that they should go through the TSCA procedures?

Dr. KARSTADT. Yes, I do, Mr. Lent. The Toxic Substances Control Act was drafted in part to increase public participation in regulatory decisionmaking. The way that the public becomes involved in a section 5 proceeding is through publication of information in the Federal Register. That would have occurred if EPA had initiated rulemaking under section 5. They did not do so. Therefore, whatever information the public has obtained has been fragmentary and very informal.

I also believe that, given the large volume of chemical and the number of unresolved questions which have been raised this morning, utilization of the regulatory authorities given to EPA is the proper manner in which to resolve the questions.

Mr. LENT. There have been so many tests and studies that have been conducted over the course of the last few years with respect to NTA. I have mentioned some of them before. The matter appears to have been rather thoroughly investigated by the Assistant Secretary of Health and Scientific Affairs, HEW, who looked at the effects. There was an International Joint Commission Task Force on NTA. The EPA risk assessment that we are talking about here today supported the same conclusions, essentially that NTA was harmless. The fact is that it has been used and tested in Sweden, Finland, and Canada.

It would seem to me that in view of this history, the exhaustive testing of the chemical over the course of 10 years, including the practical use of it over some 10 years I understand in Canada where there have been no derogatory effects, while some questions will always remain—that is the nature of science—I just do not see what practical good would come from making another 5-year study.

Dr. KARSTADT. I think the questions raised here today by Dr. Spacie and by Dr. Perry are sufficiently serious to encourage me to encourage EPA to utilize TSCA in this matter.

I went through the EPA's document, the final report on NTA, rather carefully. I, frankly, was rather surprised at the number of unanswered questions and unresolved questions, given the number of years that NTA has been in use.

Mr. LENT. Isn't it true that the Government of Canada has approved the use of NTA in detergents, as well as the Governments of Finland, Sweden, and the Netherlands? You do not believe that the governments of all of these countries would approve an ingredient if they and their scientists believed that ingredient would have an ill effect on the population, do you?

Dr. KARSTADT. I do not like to invoke extremes, but probably the most extreme case where the United States essentially escaped unfortunate occurrences encountered in other countries was the case of thalidomide. Thalidomide was used in Sweden, which we certainly hold up to be one of the most enlightened countries in regard to environmental protection.

Mr. LENT. It had not been tested, had it, in those countries? You are not comparing NTA with thalidomide, are you?

Dr. KARSTADT. What I am saying is that, as regards the information brought forth by EPA in the final report on NTA, I believe that the chemical—at least according to the questions raised in the document—has not had all the questions resolved.

Mr. LENT. Let me ask Dr. Rall a question.

Do you feel that the Canadian NTA health data is useful based on 10 years of practical experience using NTA in detergents in determining what the health effects of NTA might be in the United States?

Dr. RALL. Not at all, sir.

The primary potential problem with NTA is bladder cancer. Bladder cancer takes 20 to 30 years to develop.

Mr. LENT. This is where you ingest a chemical.

Dr. RALL. That is right, as is happening in Canada today at an average of about 3 ppb. We just do not know. We really will not know probably for another 20 years, because such epidemiological studies would be extraordinarily difficult to do. Although it is very tempting to say the Canadians have used it for 10 years, it really does not mean much.

I am not an ecologist, nor do I know anything about degradation of NTA in sewage plants, but I have been disturbed by the testimony of the first two speakers of this panel. The concept that NTA is a low risk carcinogen is based on the concept that the U.S. population will ingest no more than approximately 3 ppb. That, in my opinion, would not pose a great risk for the United States.

Mr. LENT. The one test we are all relying on is the National Cancer Institute testing back in 1977. As I understand it, they were conducted by feeding to rats and mice highly exaggerated levels of NTA; is that correct? It was equivalent to about 8 million gallons of water every day for a human being.

Dr. RALL. Because of statistical problems, that is the only way we can determine whether a compound is carcinogenic.

Mr. LENT. The cancer that developed in these rodents was not a mutagenic cancer; it was a urinary tract cancer. Isn't that correct?

Dr. RALL. Urinary tract cancers can be mutagenic.

Mr. LENT. In your testimony you said earlier that there was no evidence that NTA was a mutagen.

Dr. RALL. That is right, but, remember, the state of the art of mutagenesis is such that the best tests that we know of still only detect 90 percent of the mutagens. It is possible that NTA might

well be in that 10 percent which has not been identified as mutagenic.

Mr. LENT. Isn't this one of these unfortunate examples where you take an excessively exaggerated dosage level and find that it produces a result that bears no relationship to what happens in the real world?

Dr. RALL. Except, Mr. Lent, when you go back in history, you find that many of the carcinogens that we now know are carcinogenic in man were first detected by that method, by using a very high dose in experimental animals. It is the only method we have to detect carcinogens amongst the literally tens of thousands of compounds we have.

Mr. LENT. When the NCI conducted their test, first they used the equivalent of an individual person consuming about 8 million gallons of water each day for an entire lifetime, the rodent equivalent.

Dr. RALL. At what concentration in what—3 ppm?

Mr. LENT. I do not know what it was.

Dr. RALL. That is critical.

Mr. LENT. Maybe you can explain it to me. I am trying to learn about it.

Dr. RALL. If the NTA is in drinking water at 3 ppm, then that is much closer to the about 10,000 ppm that was in the NCI bioassay test. That gives you a safety factor of only 3,000. The risk would be a 20- or 30-percent chance for the population, all the population, to develop renal cancer. That to me is very serious.

Mr. LENT. Are you familiar with that NCI testing?

Dr. RALL. Yes, sir.

Mr. LENT. Wasn't there a point in that testing when they reduced the level of NTA being fed to the laboratory animals? As I understand it, it was reduced from the equivalent of 8 million gallons of water every day for a lifetime down to 80,000. It was reduced significantly.

Dr. RALL. No; the protocol was not changed. The standard test method is to set up different groups of animals with a high dose, a middle dose, and a low dose. The low dose animals did not show a statistically significant carcinogenic effect.

Mr. LENT. What would that lead you as a scientist to conclude?

Dr. RALL. It is a carcinogen. There were only 40 to 50 animals in that group. If you were looking for a 5-percent incidence of cancer, which is a very high incidence of cancer statistically, you would not find it in a group of 40 animals. This is a very complex thing. Let me try to explain what I am trying to say.

Mr. LENT. I realize my time is almost up. I did have a few other questions I wanted to ask some of the other witnesses.

Dr. RALL. I will be glad to try to answer if you wish.

Mr. LENT. If you would like to elaborate, go right ahead.

Dr. RALL. Let me elaborate for a minute. Suppose you wanted to know the sex of the people in the United States by a statistical sampling survey and you realized there was a body called the House of Representatives. Wouldn't you think the Representatives would be representative of the United States? Therefore, you would sample one or two people. You found they were all male. You would decide that everybody in the United States was male.

That is really what we are trying to do when we take a random group of animals, some highly susceptible to a carcinogen and some highly resistant. If you have only five animals, you will be able to detect only a cancer that gets every animal. If you get 1,000 animals, you can still detect only about a 3-percent incidence, which would be again catastrophic if the whole population were exposed.

It is a statistical problem that is very real, indeed. Maybe I have answered too much now.

Mr. LENT. I have one final question. Didn't the EPA come to a diametrically opposite conclusion from what you have come to? They assumed that there was no threshold level for NTA and that the risk was so low that its use was acceptable. What is your opinion of that EPA decision?

Dr. RALL. I am not saying anything different really than EPA.

Mr. LENT. They said it was OK and you are saying it is not OK.

Dr. RALL. I am saying, as I said in the last few words of my statement, that if the levels in drinking water are at the 3 ppb range—and that is really critical, and the two people to my left, Dr. Spacie and Dr. Perry, I think have raised some doubts about it—then it certainly is a low risk proposition. As a scientist I cannot in an expert scientific capacity advise the public what to do. It is a low risk, however. I think that is what EPA and I are both saying.

However, if more NTA escapes the various degradation processes, then it may not any longer be a low risk problem. As Mr. Maguire was discussing earlier, we must look at benefits. I do not know about the benefits of NTA.

My statement and EPA's I think are really quite consistent.

Mr. LENT. I have no further questions. Thank you, Mr. Chairman.

Mr. MOFFETT. I am really concerned about the impact of NTA on ground water. The subcommittee that I am privileged to chair over on the Government Operations Committee is getting into the ground water question and ground water problems. We have found, as I recall, that 50 percent of all U.S. citizens rely on ground water for drinking water. Many of these wells are located in areas where septic tanks are used for household water disposal. Apparently some 20 million homes rely on septic tanks.

What I would like to know from any of you is what your best scientific judgment is about whether NTA will be broken down by septic systems. Could NTA be stored in septic systems? What impact may NTA have on ground water overall?

Dr. Spacie, Do you want to respond to that first?

Dr. SPACIE. I think there is some evidence that NTA will degrade in properly working septic systems, but the degradation seems to be much slower than it is in ordinary municipal treatment.

In the Canadian monitoring study they found 1 in 21 wells that had a much higher level of NTA in the ground water than what the national average was or what typical levels were. In that one case it was a well that was relatively close to a flooded septic field. I think there is evidence that it can get into ground water. It may be degrading, but perhaps not very rapidly.

The Canadian monitoring has shown for the time that they have looked at it that the levels do not appear to be increasing, but there are detectable levels there in ground water situations.

You are quite right that situations where you may have contamination of ground water are ones to be concerned about.

Mr. MOFFETT. Does anyone have anything to add to that?

[No response.]

Mr. MOFFETT. Dr. Perry, on page 3 of his testimony—do any of you have Dr. Perry's testimony nearby or in front of you? I would like to ask Dr. Rall a question regarding that.

On page 3, do you notice down where he says, "With the same level of NTA in Western European detergents and a similar average degree of biodegradation, I would anticipate the following," under (c) he talks about the number 300. Is that right?

Dr. RALL. Yes.

Mr. MOFFETT. Then down a little farther he talks about 3,000. If I hear you correctly in response to Mr. Lent's questioning, you are saying, "Maybe it is not 3 and, if it gets over 10, I start to get a little worried." How worried do you get if it is 300? How worried do you get if it is 3,000?

Dr. RALL. I think if it were 300 or 3,000, I would be very worried, indeed.

Mr. MOFFETT. If we look at this subcommittee report, Review of Procter & Gamble's statement regarding carcinogenesis of NTA for the Executive Committee of the national toxicology program, on page 2 it says, "Drinking water supplies in Canada were found to contain an average of 2.8 parts per billion."

It seems to me this is the assumption they were operating under, which is not really a terribly valid assumption. Is that correct, Dr. Perry?

Dr. PERRY. This really reflects the whole problem—the tremendous dilutions that are being achieved in Canada as compared to many other places in the world. There is a Canadian paper which states that if NTA was not degraded at all in terms of its discharge into the St. Lawrence, it would not be a problem. That is not the situation in many other parts of the world.

I believe that these calculations really show the magnitude of the problem as it really exists in a city like London or a city that reuses its water supply.

Mr. MOFFETT. Thank you, Dr. Perry.

Dr. Rall, you have been before subcommittees that I have sat on before. I have always felt that you have been an excellent witness and very forthright and candid. I want to ask you about this EPA letter to Procter & Gamble.

It is effectively an advisory opinion, as I understand it, that indicates the Agency is not taking regulatory action against NTA. Are these kinds of advisory opinions unusual in the health and safety field as far as you are concerned?

Dr. RALL. I guess my response is I do not know. I guess that means they must be unusual. Typically there is a more formal process.

Mr. MOFFETT. Thank you, Mr. Chairman. I hope perhaps we will have another opportunity to question on a second round. I yield back the balance of my time now.

Mr. MAGUIRE [presiding]. Mr. Dannemeyer?

Mr. DANNEMEYER. Members of the panel, I am not a scientist. I am probably not qualified to evaluate or attempt to second-guess what the members of academia have said.

However, I would be interested in having your evaluation of where you feel the EPA went astray in reaching the conclusion that has brought you here today. They are supposed to be equally adept in the academic process as you in evaluating risks or protecting the health of people.

If I understand correctly, the EPA has said that they have weighed the risks and they want to let these folks go ahead with this thing. I would like to know where did the EPA go wrong in these terms:

First of all, are the facts on which the EPA is basing its posture wrong? If so, where? If you agree that their facts are correct, then I guess you are saying their judgment is wrong. If you point that out, please indicate what that fallacy of judgment is?

Dr. SPACIE. I will give it a try. I do not think the facts are wrong or the conclusions that they have come to in the risk assessment are wrong, at least from the environmental point of view, which is the part that I read. We are in basically complete agreement with what they said in that.

I would think that it is a matter of opinion whether you prohibit something until all questions are settled or whether you allow it to be produced while questions of this sort are being settled. That is not the kind of decision that I could answer.

As far as the facts on the environmental effects are concerned, they are in agreement with everything that we have seen.

Mr. DANNEMEYER. Do any of the other members of the panel wish to respond?

Dr. RALL. The health effects part of the review is essentially correct. I have no problems with that.

I think the issue that is developing in the past few minutes is whether the assumptions about the average ingestion, which appear to be true for Canada, will apply to the United States, which is a very different country than Canada. We have a much higher population density. We use our water much more extensively.

The one thing I would very much want to see if NTA is reintroduced into detergents is a very intensive survey of the concentration of NTA in the water supply. That really becomes absolutely mandatory.

Dr. KARSTADT. My research interest these days centers on estimating exposure to chemicals. I am usually interested in workplace exposures.

What is developing in this discussion today here is concern about the estimates of exposure to NTA for both environment and humans. As Dr. Rall mentioned, there are questions about the applicability of the Canada data, which may well be valid for Canada, to this country.

What I am concerned about, based on experience in the workplace, is what you might call microenvironments—whether you can generalize to the large scale from observations made in a smaller situation. For instance, if we know there are situations under

which NTA degrades well, are those situations sufficiently common in the United States so that we can set an average exposure level and feel confident about it?

Assessing risk for either the environment or for human health really will depend on having a good estimate of exposure. What I am concerned about is making sure those exposure data are good.

Dr. PERRY. I would like to stress again the nonapplicability of the Canadian experience. According to the European environmental program, in which I am involved, the usage of NTA in the other countries cited—namely, Sweden and more recently in Holland—is extremely low. It is a very small percentage of the market. The problem, therefore, is that no real experience exists in monitoring this material in a water reuse situation.

I further submit that the way in which average data for plant performance have been used is scientifically invalid in that the variations in these data are extreme. For example, we carried out pilot plant studies on NTA in sewage at the 10 ppm level. We acclimatized the sewage treatment plant to degrade that material. We then increased the level just from 10 up to 20 ppm, double, a typical washday-type situation. In that situation there was a 200-percent increase in the level of lead in the effluent for the first few hours after increasing the NTA dosage.

That to me is something which has been evaluated at the pilot plant level only. It is so serious in my opinion that it needs a detailed major sewage treatment plant investigation. Unfortunately, none of the plants in Canada have been monitored in that way. Much of the data presented have been obtained from samples which have not even taken account of the hydraulic retention of the works involved.

Mr. DANNEMEYER. Mr. Chairman, all of the panelists have testified as to their reservations about the EPA and the studies which led it to approve NTA. I understand that several other distinguished scientists were invited to testify but their schedules would not allow it. I would be interested to know whether their testimony would reinforce or dispute that of this panel. It would be helpful to obtain written statements from them.

They are: Dr. Arthur Upton, the New York Medical Center, formerly Director of the National Cancer Institute; Dr. John Weisberger of the American Health Federation Institute of Disease Prevention; and Dr. George Becking of Canada, Acting Director of the Bureau of Chemical Hazards, Canadian Department of Health and Welfare.

I would ask unanimous consent that written statements, or a copy of official policy in the case of Dr. Becking, be requested from them and be included in the record of this hearing.

[Invitations were extended to Dr. Weisburger, Dr. Upton, and the Department of Health and Welfare of Canada to submit statements for the subcommittee's hearing record. The following two statements were received in response to the subcommittee's request.]

*Bill Dunnington - a career biochemist
about this and he agreed for me to submit this
as his statement for Commerce/Investigations having
record - as per your unanimous consent requested*

AMERICAN HEALTH FOUNDATION
NAYLOR DANA INSTITUTE FOR DISEASE PREVENTION
Dana Road, Valhalla, New York 10595 Telephone: 914-262-1900

Jim Martin

June 24, 1980

LB

American Health Foundation
200 East 43rd Street
New York, New York 10017
Telephone: 212-953-1900

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Vice President for Research
Naylor Dana Institute

Hon. James G. Martin
U.S. Congress
341 Cannon Bldg.
Washington, D.C. 20515

Dear Mr. Martin:

Re: Nitrilotrisacetic acid (NTA)

While I was director of the bioassay segment of the NCI, I was asked to comment on possible safety problems with this chemical. Because of a number of problems associated with phosphate, utilized extensively in the detergent industry, namely eutrophication of waterways, nitrilotrisacetic acid (NTA) was developed as a substitute. The advantage of this material was that it did not lead to eutrophication, and more importantly that it could be degraded rather completely during the normal processing in sewage treatment facilities.

The structure of the chemical did not suggest that it would have any kind of adverse effects. It is highly water-soluble, and just like phosphate, it is a good chelating agent. Also, NTA is not mutagenic as such, nor after metabolism.

Because of the potential of widespread use and, thus, possible human exposure even at low dose levels, it was decided to submit this chemical to the standard bioassay test which we developed. This involved exposure to the maximally tolerated dose (MTD), and 50% of that dose. In addition, for an entirely different reason and approach, Dr. Richard Bates, then in the Pathology Branch of NCI, entered NTA into a test series utilizing slightly different protocols.

The results of our test series, as well as that developed by Dr. Bates indicated that at levels of 20,000 and 15,000 ppm in the diet, NTA induced

NAYLOR DAHA INSTITUTE
DISEASE PREVENTION

Hon. James G. Martin

- 2 -

June 24, 1980

cancer in the kidney and the urinary bladder in mice and rats. However, the response fell off very sharply at lower dose levels. In our test, utilizing a dose of 7,500 ppm, 50% of the maximally tolerated dose, there was a lower incidence of kidney and bladder cancers. At even lower dose levels, such as used in the series developed by Dr. Bates, the incidence was not significantly different from that of control animals.

A careful and objective evaluation of these results suggested that NTA could not be considered to be a "carcinogen", despite the fact that cancer was induced in two species. The reasoning behind this conclusion is the peculiar dose response, the organs affected, and the fact that this material, in our experience, had a structure such that it was unlike any of the known aliphatic or aromatic/heterocyclic molecules known to cause cancer in animals or in man. Also the data in the rapid bioassay systems, such as mutagenicity testing were uniformly negative.

In fact, in structure and properties, NTA is like EDTA, freely used in the public domain, including in foods. We used EDTA as a control, and found it to be more toxic than NTA, so that a lower MTD dose had to be used with EDTA than with NTA.

We know of other cases where kidney and/or bladder cancers stem from a metabolic artifact. For example, ethylene glycol, a widely used industrial chemical and solvent, has led to kidney and bladder cancers because of its metabolism to oxalic acid and related metabolites which tend to crystallize in the kidney and, thus, lead to cancer. High levels of a material proposed for food use, MYR-45, does likewise.

It would appear that NTA, an excellent chelating agent, can form insoluble matter in complexes with calcium, magnesium, and zinc. At high levels - but not at low levels - these might form overt or occult crystals, which in turn may lead to cancer through unspecified solid state mechanisms.

It is quite clear that this particular reaction sequence did not at all operate with lower dose levels, thus explaining why cancer was seen mainly with very highest



dose levels. Obviously with lower dose levels, the chelates are at concentrations below the solubility products and are, therefore, excreted without difficulty. Thus, with this mechanism it is quite certain that the use of this material as an ingredient in detergents does not constitute any risk whatsoever, especially since the concentration of this material would decrease through bacterial metabolism in sewage treatment plants and waterways.

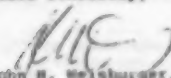
To the uninitiated, NTA is an unusual compound since in the specific protocols it caused cancer in two species. Thus, as you will note in the attached letter, I congratulated the Administrator of the EPA, Mr. Douglas M. Costle, and his assistant, Mr. Steven Jellinek, on the basis of taking sound advice that the planned use of NTA in the detergent industry did not constitute a general human cancer risk.

We need public servants who can intelligently interpret all of the available data base and reach sound conclusions in the public interest. In this instance they have indeed done so, and I do hope that we can all agree that the research conducted establishes NTA as beneficial and safe.

We, in medical research with emphasis on cancer, have a larger problem, namely, to account for 400,000 annual cancer deaths, with the aim of reducing the risk of these diseases. We would hope that all of those concerned with research formulation and research support would examine the current data base on causes for each kind of cancer and take the required initiatives in public health action and in research to reduce such avoidable cancer risks.

I hope these comments have been helpful to you.

Yours sincerely,



John H. Weisburger, Ph.D.
Vice President for Research

JHW:CH
att.



AMERICAN HEALTH FOUNDATION

NAYLOR DANA INSTITUTE FOR DISEASE PREVENTION

Dana Road, Valhalla, New York 10595 Telephone: 914-262-2000

May 30, 1980

American Health Foundation
270 East 42nd Street
New York, New York 10017
Telephone: 212-652-1000

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Charles E. Arnold, M.D., M.P.H.
Vice President for Research
Nutrition Institute

Mr. Douglas M. Costle
Administrator
Environmental Protection Agency
401 M Street, SW
Washington, D.C. 20460

Dear Mr. Costle:

Subject: EPA Action on NTA

Congratulations! Your Agency has used good advice and it has made the proper decision in allowing NTA to be used in the detergent field as an effective substitute for phosphate.

I was at NCI when we designed the tests to determine whether NTA was safe. From various lines of evidence based on sound theoretical mechanisms, I always thought NTA was safe. Thus, when the high level feeding showed that animals had urological tumors, we examined the reasons for such tumors and found that tumors were due to an artifact, probably of crystalluria of insoluble complex salt which would not be found under low level actual use.

We have discussed these and other matters bearing on basic mechanisms of carcinogenesis in a review in Casarett & Doull's TOXICOLOGY which your staff may consult to verify, indeed, that your Agency has used the best in medical science and arrived at the proper conclusion.

As a medical scientist concerned with cancer research for 30 years, I am heartened by the fact that Federal officials are able to make judicious interpretations of a complex field and come to the right conclusion in the best interest of the people.

Sincerely,

John M. Weisburger
John M. Weisburger, Ph.D.
Vice President for Research

JMW:hls
cc: S. Jellinek



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Mr. Bob Eckhardt,
Chairman,
Subcommittee on Oversight and
Investigations of the Committee on
Interstate and Foreign Commerce,
House of Representatives,
Congress of the United States,
Room 2323,
Rayburn House Office Building,
Washington, D.C. 20515
U.S.A.

Dear Mr. Eckhardt:

Thank you for your letter of July 15, 1980, in which you extended an invitation to Dr. George Becking of the Health Protection Branch to make a statement for the record of the June 26, 1980, hearing of the Subcommittee on Oversight and Investigations of the Committee on Interstate and Foreign Commerce, on the Environmental Protection Agency (EPA) action concerning nitritotriacetic acid (NTA).

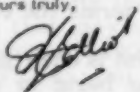
The Canadian point of view on the safety of NTA is well-known world-wide. All of the scientific data used in arriving at the decision that NTA poses no health risk has been presented to the International Joint Commission's Task Force on the Human Health Effects of NTA and to other governments upon request. During the past year, EPA officials were made aware of the scientific information upon which the Canadian position is based. I might add that scientific data presented to this Branch since making our original health hazard assessment has only reinforced our opinion regarding the lack of health hazard from the levels of NTA currently found in the Canadian environment.

... 2

Mr. Bob Eckhardt

It is my understanding that your Subcommittee addressed both the scientific data available on NTA and the appropriateness of the regulatory action of EPA regarding the use of this chemical in laundry detergents. I have already commented on the availability of the scientific data on NTA and the present Canadian position regarding the use of this chemical, but I still feel that present government policy precludes a response to your request for an official statement on NTA from Dr. Becking.

Yours truly,


for A.B. Morrison, Ph.D.,
Assistant Deputy Minister,
Health Protection Branch.

Mr. DANNEMEYER. I have no further questions.

Mr. MAGUIRE. We will pause for 10 minutes and then come back.
[Brief recess.]

Mr. MAGUIRE. The subcommittee will come to order.

Dr. Perry, you have made some statements about the different behavior of NTA in different types of waters. You have indicated that you think the situation in Canada where the concentrations were on the average 3 ppb underestimated the kinds of concentrations that would be found in Western Europe. I wonder if you could be a little more explicit about what you think the extrapolations might be for the United States, particularly for the more heavily populated Midwest or northeastern part of the United States, with respect to NTA levels. Are you in a position to make any guesstimates on that?

Dr. PERRY. I would not like to quote definite figures on that, Mr. Chairman. I have traveled extensively in the United States, but I only know in general terms the extent of the problem as I would see it.

I think the valid point is one really which Dr. Spacie raised. I see the major problem as being in areas such as California where water reuse is practiced significantly. Clearly, I know about plants like the Lake Tahoe plant, which has pioneered chemical treatment work. My reservations clearly would relate to that type of situation.

I do not have the figures, however, on the extent of water reuse in the United States.

Mr. MAGUIRE. Are the members of the panel reasonably satisfied that we have a different kind of situation with respect to NTA levels where water is salty, where it may be polluted and therefore anaerobic, where we may be dealing with sewage treatment plant processes, where we may be dealing with pH factors that are not normal? Would any or all of you care to comment on that?

Dr. PERRY. May I make one further comment?

Some of our laboratory studies have indicated that there are problems in the biodegradation of NTA in soft water situations.

Mr. MAGUIRE. In which—salt water?

Dr. PERRY. Soft water.

Mr. MAGUIRE. There are problems in soft water situations?

Dr. PERRY. Furthermore, this degradation process depends very much on the numbers and types of heavy metals that are also present in the water. Again, I have no figures for the United States to indicate how many soft water areas there are. This certainly is an area that needs further investigation.

Mr. MAGUIRE. You have said that the questions of heavy metal transport through a sewage treatment plant in soft water areas has not been sufficiently analyzed. Are you suggesting that the metallic pollution of the receiving waters might render them unsuitable as a source of potable water?

Dr. PERRY. May I just take a case in point?

If nondegraded NTA is present in a receiving water its degradation depends upon the form of complex in which it exists—in a hard water area this would be possibly a calcium salt of NTA. If, however, there were other metals present, and in particular metals like cadmium, the resulting cadmium salt of NTA would not de-

grade at all. This is a problem that in my opinion has not been adequately studied in a real world situation.

Mr. MAGUIRE. Would you say that the EPA analysis as you have reviewed it has not adequately taken this into account?

Dr. PERRY. I would say that is true, yes.

Mr. MAGUIRE. If I understand your testimony correctly, you are saying that it does not really answer all the questions you might have to review the biodegradable characteristics of NTA under what might be described as ideal conditions. Rather, they ought to be reviewed under what might be described as more realistic. Is that correct?

Dr. PERRY. That is correct.

Mr. MAGUIRE. Do any other members of the panel want to add a comment on this point?

[No response.]

Mr. MAGUIRE. Dr. Spacie, you indicate that your task force has examined a number of builders that may serve as alternatives—citrate, carbonate, silicate. You are also looking at two other organic compounds—CMOS and CMT. Can you tell us a little more precisely where that investigation stands with respect to effects on the environment of those alternatives to NTA?

Dr. SPACIE. First, I should say that we looked at each one individually really. We did not make an attempt to pick the best out of five or anything like that. We just looked at each one individually.

The NTA report is out, of course. The report on the other organic builders will be out in about a month and a half. I think I have summarized our overall findings on those builders.

The report on the inorganic builders is not yet available. We are still working on that.

Mr. MAGUIRE. Have you looked at the question of how well these different compounds wash clothes?

Dr. SPACIE. No. We are not dealing at all with performance. That is another matter. We are looking at degradation in the environment, possible toxicity to organisms, and that sort of thing.

Mr. MAGUIRE. I notice that in one of the statements that we are going to have later there is a statement to the effect that "The Science Advisory Board of the Canadian-United States International Joint Committee for the Great Lakes has 'approved' the use of NTA in detergents."

You have been associated with that Joint Commission. Is that your understanding?

Dr. SPACIE. We really do not have any direct powers to approve or disapprove anything in a legal sense. What our report says is that at this time we see no reason to prohibit production of NTA. Then we have listed our reservations, which were the ones I gave in the statement. That is not approval in any sort of official capacity.

Mr. MAGUIRE. Dr. Rall, in the EPA report the issue of potential carcinogenic daughters and/or granddaughters is raised and then dropped. IDA, aminodiacetic acid, is an intermediate of NTA biodegradation. Associated with IDA is NIDA, N-nitroso-aminodiacetate, which is believed, as I understand it, to be carcinogenic in mammalian species.

The report goes on to note that most studies demonstrate the improbability of IDA accumulation during NTA biodegradation in nature, because of the rapidity of NTA's biodegradation. It is clear, however, from the Canadian experience that the widespread use of NTA will result in a constant level of NTA in our water systems. This will occur when an equilibrium point is reached between the amount of NTA entering the water system and the rate of biodegradation. It would seem likely, therefore, that a constant level of NTA would yield a constant level of IDA and NIDA.

On page 13 of the EPA report, the potentially serious question of NIDA accumulation is raised but then dropped. However, the biodegradation properties of NTA itself are admittedly linked to the oxygen content of the water and to water temperature, among other things.

I wonder if, in light of all this, you are satisfied that NIDA will not accumulate in cold anaerobic water environments or is there a question in your mind on that point?

Dr. RALL. I just do not think at this point in time, Mr. Maguire, we know. Again, I would think this would be a very appropriate study to do, so that we can satisfy ourselves as to whether or not this is likely to occur.

IDA and NIDA are relatively nonstable, but I would prefer not to speculate. I would prefer to see the evidence one way or the other as to whether they are there.

Mr. MAGUIRE. But it does conceivably complicate our task here in analyzing the possible health and environmental effects of given levels of NTA retention in given types of water systems, does it not?

Dr. RALL. It does, but I think that could be settled fairly rapidly and straightforwardly.

Mr. MAGUIRE. How would you settle it?

Dr. RALL. In the proper circumstance of cold anaerobic environment to see whether any IDA or NIDA could be detected.

Mr. MAGUIRE. Would you do that before or after you put the product on the market?

Dr. RALL. I am a great believer in the Toxic Substances Control Act which suggests these studies should be done before the product is marketed.

Mr. MAGUIRE. Dr. Karstadt, do you have any comment on this particular point?

Dr. KARSTADT. No, I don't, Mr. Maguire.

Mr. MAGUIRE. Does anybody else?

[No response.]

Mr. MAGUIRE. Dr. Rall, apparently a conversion factor of 5.85 was used by EPA in extrapolating from the animal data to the risk assessment for human populations. I wonder if you could tell us how this compares with conversion factors used in other studies with which you are familiar.

Dr. RALL. That conversion factor is based on some research that I was deeply involved in many years ago as well as theoretical consideration.

If you look at the toxicity of chemicals to laboratory animals and to man, you will find that systematically the mouse is on the average able to tolerate more chemical on a milligram per kilo, on

a per weight basis than is the rat. The rat is able to tolerate more than man. This is roughly proportional to the surface area of each of these three species.

To put it another way, if you talk about milligrams of compound ingested per unit surface area, the toxicity for mouse, rat, and man is surprisingly consistent over about 20 toxic compounds where we have very good data. This conversion then is approximately the conversion factor of about six, which is the rat-to-man conversion.

There are theoretical reasons why surface area might be more relevant than body weight—the so-called scaling-up problems. A bigger airplane is not exactly the same as a smaller airplane. It has different characteristics.

That is an appropriate use of that conversion factor. It builds in no safety factor, but the use of the confidence limits should build in a safety factor.

Mr. MAGUIRE. Are higher conversion factors used in some other cases with specific compounds?

Dr. RALL. Safety factors can be built in, but in this instance the so-called upper 95-99 percent confidence levels were used. I am not a statistician. That simply says statistically the numbers for the percentage of tumors found will vary on a random basis, and 95 percent of the time they will be within this limit and 99 percent of the time a slightly higher limit.

Mr. MAGUIRE. What would have been an appropriate safety factor in your judgment to have used in this instance?

Dr. RALL. I do not think anyone knows. Remember, in the history of trying to convert laboratory animal toxicity to projections for human toxicity, our first approach was to use safety factors and not try to make any of these quantitative comparisons. Safety factors for compounds which did not have what I call long-term irreversible, progressive effects, such as cancer, were in the order of 10 to 100.

It had been proposed some time ago that safety factors in the order of 5,000 might be used for a carcinogen. Theoretically, although there are many problems with risk assessment, I think we have to go through the process.

It is intellectually appealing to try to make the best point estimate of what the anticipated excess incidents of cancer will be. That is a point estimate. It has no safety factor built into it. If man happens to be more sensitive, then that will underestimate the risk. If man is less sensitive, it will overestimate it.

Mr. MAGUIRE. Do we know in this case whether man is more or less sensitive to NTA?

Dr. RALL. No, we do not.

Mr. MAGUIRE. Would it be a wise regulatory policy, once you have made the best scientific judgment that you can make on what you call the point factor, to try to build in some sort of a safety factor in the policymaking process?

Dr. RALL. I think so, but I do want to emphasize that we are just in the middle of constructing intellectually this way of trying to estimate risk. It is really in a state of discussion amongst the scientists.

Mr. MAGUIRE. One of the questions that has been raised, of course, is the possibility of the existence of a threshold. Would it be

generally considered now, given what we know, that this is a hypothesis that has yet to be demonstrated or do we in fact have the ability to identify a threshold in this case?

Dr. RALL. From the evidence I have seen with NTA, I think it is possible, indeed, that there may be a threshold. It does seem to be a slightly different type of carcinogen than many that we are used to dealing with. The evidence simply has not yet been presented to show that that is anything more than a reasonable hypothesis. Studies could be performed which would either very much strengthen or weaken that hypothesis. However, they have not yet been done.

Mr. MAGUIRE. If there is a threshold, do we know enough to set it?

Dr. RALL. No, not now.

Mr. MAGUIRE. In an interview with Dr. Robert Goyer, who I believe works with you, he indicated that the detergent program at P. & G. might also wish to use zeolites along with NTA, and that such a combination might be harmful to the kidneys. Do you have any comment on that?

Dr. RALL. No. I think I would agree with Dr. Spacie that the issue of the zeolites is something that is still being investigated. We really cannot comment yet.

Mr. MAGUIRE. We asked Mr. Jellinek at EPA about the consultative process that he went through or failed to go through with respect to the decisions that he made on this matter. He indicated that on May 23, 1980, he met with you to discuss a number of EPA and NTP issues, and that in the course of that meeting you "reviewed a draft of the letter that was subsequently sent to Mr. Krumrie on May 27, 1980, to inform Procter & Gamble of the agency's position on NTA."

I am wondering from your point of view exactly what occurred at that meeting. Did you approve the draft letter? Did you look at it and comment? Did you look at it and not comment? What kind of a consultative process was this, Dr. Rall?

Dr. RALL. We met clearly for other purposes. By that time it was quite late in the afternoon, like 6 o'clock. I looked at it. I haven't the vaguest idea what my precise comment was. I did read it in a quick and hurried manner. That really was not a consultation of the sort that would allow any review of the proposal.

Mr. MAGUIRE. Did he ask you for your approval or disapproval?

Dr. RALL. Not to my knowledge.

Mr. MAGUIRE. Did he ask you to review it in any formal way with your staff?

Dr. RALL. No. I do not even think I had a copy of the letter when I left the office.

Mr. MAGUIRE. Dr. Karstadt, if EPA had initiated rulemaking under section 5 of TSCA, as you have suggested ought to be done, would you expect that relevant scientific, public, and other agencies of government as well might have been more fully consulted than was in fact the case?

Dr. KARSTADT. I would expect that to have occurred, at least in part because of the procedures prescribed by the Toxic Substances Act for rulemaking under section 5, since the act requires that if a manufacturer wants to market or process a "significant new use"

of existing chemicals, what amounts to a notification similar to the premanufacture notification has to go in to EPA. That notice is then published in the Federal Register, which gives the public information on the proposed use of the chemical. The public would be brought in at that point. Scientists in groups that might wish to comment would have a chance to participate in decisionmaking then.

There is also a very important provision in the Toxic Substances Control Act under section 9, a subsection called "Coordination."

Section 9(d) essentially provides for coordination of EPA's activities with other responsible agencies, including what was then the Department of Health, Education, and Welfare: "For the purpose of achieving maximum enforcement of this act while imposing the least burdens of duplicative requirements of those subject to the act and for other purposes."

I would assume that because of the intent of the Toxic Substances Act, if formal rulemaking had been initiated there would have been more of a tendency on the part of EPA to consult with other agencies within the Government.

Also, the EPA belongs to the Interagency Regulatory Liaison Group and is represented on the executive board of the national toxicology program, of which Dr. Rall is the head. I would assume that if a formal rulemaking were contemplated or if EPA considered NTA to be a serious problem, it would have been taken and perhaps should have been taken up in those bodies, inasmuch as there were policy questions of various sorts involved.

Mr. MAGUIRE. Would you regard it as a requirement of the law that that be the case or simply advisable under the procedures suggested by TSCA? How would you characterize it?

Dr. KARSTADT. Reading section 9(d), the mandatory language is in there. It says "shall consult and coordinate with the Secretary of Health, Education, and Welfare and the heads of any other appropriate Federal executive department or agency."

Mr. MAGUIRE. Dr. Rall, would you have thought that this was the kind of decision that ought to have been referred to the Interagency Regulatory Liaison Group and/or the national toxicology program for more formal review?

Dr. RALL. Certainly in a sense it had been discussed at the NTP executive committee. The review that I quoted from in my opening statement was created by a subcommittee of that executive committee.

Mr. MAGUIRE. I am talking not about the review of the literature. I am talking about a review of the regulatory decision that was in fact made on the 27th of May and communicated to Procter & Gamble.

Dr. RALL. As a general principle, the more input you have into a major and critical decision such as that, the better the decision will be in the long run. I would have thought an appropriate way would have been to discuss it with some of the heads of the other health research and health regulatory agencies.

Mr. MAGUIRE. Members of the panel, in a statement that we are going to hear soon from John Pepper of Procter & Gamble he refers to NTA as "a safe ingredient." I wonder if that is a charac-

terization which any of you would accept based on the knowledge that you have.

Dr. PERRY. I would certainly not accept that at all.

Mr. MAGUIRE. Dr. Spacie, you have not differed in some respects with the EPA analysis. Would you accept the description that NTA is "a safe ingredient?"

Dr. SPACIE. I am not really clear on what they mean by "safe." It is obviously something that is subject to statistical problems. I do not think that is the kind of statement I can make one way or the other.

Dr. KARSTADT. I think the question of safety is both a scientific and a social judgment and implies consideration by both scientists and persons representing the public at large. I would not be in a position to make such a judgment. I would have reservations based on the questions EPA has raised and based on the questions raised by Dr. Spacie and Dr. Perry this morning.

Dr. RALL. I had hoped that we were out of the era when we would indiscriminately label things as safe or hazardous. Certainly a compound which can cause cancer—does cause cancer in laboratory animals, and I do not think there is any question about that—just cannot be called safe. We simply have to get more sophisticated from this safe or nonsafe approach to things.

Mr. MAGUIRE. Mr. Lent, do you have any further questions?

Mr. LENT. I just have one question for Dr. Perry who comes over from the United Kingdom.

Doctor, do you know whether the EPA had the benefit of your studies on this subject at the time they issued their risk assessment document?

Dr. PERRY. No, I don't know.

Mr. LENT. As I understand it, are you a coauthor with a Dr. Stoveland on a study involving the removal of NTA in a laboratory system operated with either hard water or soft water?

Dr. PERRY. Yes, Dr. Stoveland was one of my Ph. D. students.

Mr. LENT. Perhaps you can correct the record if I am wrong, but I believe that your study was part of the bibliography of the EPA study that was evaluated along with studies by Jones and Vashon. Are you familiar with that study?

Dr. PERRY. No.

Mr. LENT. Jones and Vashon also studied these hard and soft water questions with respect to NTA and came to a somewhat different conclusion than the Perry-Stoveland study.

Are you familiar with the Forsberg and Lindquist study?

Dr. PERRY. Yes.

Mr. LENT. Can you tell us what that study concluded with respect to hard and soft water effects on NTA? Did that not come to a different conclusion than your study?

Dr. PERRY. I think it emphasized the point that the NTA degradation was dependent upon the metal complex that was present.

Mr. LENT. The study indicated that NTA-consuming microorganisms grew on NTA in very soft lake water at 10, 50, and 100 milligrams NTA per liter and 7 to 11 milligrams calcium. Is that correct?

Dr. PERRY. I haven't got the paper before me. I will take your word on that.

Mr. LENT. Are you familiar with the Thompson and Duthie study?

Dr. PERRY. I couldn't quote from it from memory. We have reviewed a lot of these.

Mr. LENT. Is it fair to say that their study concluded that NTA degraded at about the same rate and extent as glucose, which is a very fast degrader?

Dr. PERRY. The emphasis of a lot of these studies is the one that I have really tried to emphasize in my testimony. I am not disputing biodegradation of NTA under strictly controlled conditions. What I am disputing is the biodegradation of NTA under variable load conditions and variation of temperature.

Our experience in the laboratory has shown that under soft water conditions, using the same laboratory simulation studies that the detergent industry use to study biodegradability, we have had great problems in getting NTA to biodegrade. Under hard water conditions with a changing NTA influent concentration, we have shown that although the system will eventually acclimatize to NTA, variations in load lead to high levels of undegraded NTA in the effluents. These are the factors, I believe, that are important.

Mr. LENT. The Forsberg and Lindquist, the Thompson and Duthie study, the Walker study, the Bjorndal study, came to differing conclusions than your study and found, in fact, whether we were talking about hard water or soft water, there was a very sufficient degradation of NTA.

Dr. PERRY. I do not disagree that NTA under these controlled conditions will degrade. I do absolutely dispute that it will degrade under varying influent conditions and that these problems were found in our laboratory work to be exacerbated in the soft water situation.

Mr. LENT. Thank you for that explanation. I have no further questions.

Mr. MAGUIRE. Mr. Moffett?

Mr. MOFFETT. Thank you, Mr. Chairman.

How many of you have actually read this risk assessment report?

[Show of hands.]

Three of you have. I know you were invited late, Dr. Perry, so you would not be expected to have read it.

Let me ask Dr. Spacie a question first. If you were in Mr. Jellinek's position and the request came in from Procter & Gamble, leaving aside for the moment the business of whether there is a public hearing held and those procedural types of things such as who gets to participate, what about the study itself? How would your approach have differed, if at all, from the approach that was taken here?

Dr. SPACIE. I have a particular bias toward the subjects that I do research in, which are studies on aquatic environments. Therefore, I will comment on that.

My particular view is that it is not sufficient to simply require monitoring when a product comes out at this magnitude. I have seen very many environmental monitoring programs that do not necessarily answer the kinds of questions that you want answered.

Mr. MOFFETT. They do not even require monitoring.

Dr. SPACIE. Whether they recommend it or require it.

In our report we have tried to outline some very specific types of experiments or measures that should be made under particular conditions, such as soft water, low pH, estuarine conditions. We have tried to emphasize the importance of looking at the organisms, the effect on the organisms—not just measuring presence or absence of NTA in a particular water sample. From that point of view, I would spell out more strongly what types of studies ought to be done, rather than to just make a general statement about monitoring which could be construed as going out, taking grab samples, and monitoring for presence or absence of NTA.

Mr. MOFFETT. As a professor, if this had been submitted to you as an assignment, what would you say? In other words, maybe you could play this little game in the classroom:

Procter & Gamble informed EPA they were interested in resuming use of NTA as a substitute for phosphates in their laundry detergents sold in some areas of the United States, and they asked your class to assess the present state of knowledge concerning the possible health and environmental effects of NTA. I am in your class and I submit this. How am I graded?

Dr. SPACIE. On that document we have no quarrel with the content, really.

Mr. MOFFETT. Do I get an "A"?

Dr. SPACIE. You get an "A" for the risk assessment but you get an "I," which is an incomplete, for the letter to manufacturers.

Mr. MOFFETT. That is an interesting grading system.

Dr. KARSTADT. Would you like to comment?

Dr. KARSTADT. Were I in Mr. Jellinek's position and were I presented with this document, I guess one thing I would wonder about is exactly how it was written and who wrote it. I would want to have some information even if I were grading a paper blind which assures fairness to the person whose paper is being graded.

Given the questions raised in the FRN document, given the volume of chemical which could be discharged into U.S. waters, and given a piece of legislation as potentially useful as the Toxic Substances Control Act and as little used as EPA has used it to date, I think I would certainly at least give section 5 a try and resolve some of these questions before the chemical was used.

Mr. MOFFETT. Dr. Rall, I assume you are not in the classroom but you wish that you were; right?

Dr. RALL. Very much, sir.

The concept of an "A" for effort and an "I" for the lack of monitoring is quite a good concept. I would like to endorse the professor to my left.

Mr. MOFFETT. Thank you all for your testimony.

Thank you, Mr. Chairman.

Mr. MAGUIRE. Thank you very much for your testimony. We appreciate your appearance.

The next panel of witnesses includes Dr. Richard Lehne, director of corporate regulatory affairs, Church & Dwight Co., Inc.; Mr. W. C. Krumrei, senior director, research and development, Procter & Gamble Co.; and Mr. Monte C. Throdahl, senior vice president of Monsanto Co.

Mr. KRUMREI. Mr. Chairman, before we are sworn in, may I beg your indulgence? I have Mr. Pepper with me, who is a group vice

president of our company. He would like to say a few words. I also have some experts here who can better answer some of the questions that apparently the panel would like answered.

Mr. MAGUIRE. Perhaps all of those who might be making statements to the committee could stand and be sworn in.

Mr. THRODAHL. Mr. Chairman, I also have someone with me.

Mr. MAGUIRE. Let's swear everybody in. Raise your right hands.

Do you swear to tell the truth, the whole truth, and nothing but the truth, so help you God?

Dr. LEHNE. I do.

Mr. KRUMREI. I do.

Mr. THRODAHL. I do.

Mr. WILSON. I do.

Mr. PEPPER. I do.

Mr. COWAN. I do.

Dr. WINTERS. I do.

Dr. GOLBERG. I do.

Mr. MAGUIRE. Dr. Lehne, please proceed.

TESTIMONY OF DR. RICHARD K. LEHNE, DIRECTOR OF CORPORATE REGULATORY AFFAIRS, CHURCH & DWIGHT CO., INC.; JOHN E. PEPPER, GROUP VICE PRESIDENT, AND WILLIAM C. KRUMREI, SENIOR DIRECTOR, RESEARCH AND DEVELOPMENT, PROCTER & GAMBLE CO., ACCOMPANIED BY DOUGLAS COWAN, DIRECTOR, PRODUCT DEVELOPMENT, PACKAGE SOAP AND DETERGENT DIVISION, DR. ROBERT WINTERS, MANAGER OF PROFESSIONAL AND REGULATORY SERVICES, PACKAGED SOAP AND DETERGENT DIVISION, AND DR. LEON GOLBERG, PRESIDENT, CHEMICAL INDUSTRY INSTITUTE OF TOXICOLOGY; AND MONTE C. THRODAHL, SENIOR VICE PRESIDENT, MONSANTO CO., ACCOMPANIED BY DR. JAMES WILSON, MANAGER, RESEARCH AND DEVELOPMENT, PRODUCT ACCEPTABILITY AND ENVIRONMENTAL AFFAIRS

Dr. LEHNE. My name is Richard Lehne, and I am the director of corporate regulatory affairs for Church & Dwight Co., Inc.

Church & Dwight, Inc., is the manufacturer of sodium bicarbonate and Arm & Hammer brand consumer products, including Arm & Hammer laundry detergent. Arm & Hammer laundry detergent is a nonphosphate product with a 1.3 share of total market, based on the current 52-week market survey SAMI reports, although we're only distributed in about 85 percent of the United States, with the strongest market in the Northeast where the share exceeds 3 percent. While it is difficult to estimate our share of the nonphosphate products, we feel it is about 2.8 percent.

Since the early 1970's, when the problem of eutrophication and the role of phosphates became an issue, phosphate replacements had been sought and used. These include the carbonates, citrates, silicates, and zeolites, as well as several experimental materials like CMOS and builder M.

These materials are classified as detergent builders. Detergents, whether spray dried or blended, are a combination of several materials, each with its own specific function. Builders are added to sequester—that is, to inactivate—water hardness minerals like calcium and magnesium, to keep particulate soils in suspension, to

provide alkalinity which aids in cleaning, and to allow the surfactants to perform at their maximum without forming sticky residues.

The material of choice which best performs all of these functions is sodium tripolyphosphate, and of course it is still used, although at somewhat lower levels than before, in areas where phosphates are not banned. All of the alternatives to phosphates have some disadvantages, but detergent chemists have developed formulations of nonphosphate products which are satisfactory performers. The efficacy of the builders depends upon many factors, such as water hardness, water temperature, nature of the soils and of the fabrics, and, of course, the particular surfactant system.

In soft water where calcium and magnesium are minimal and sequestering is not required, all of the built detergents are fairly comparable in performance. Carbonates suffer in hard water by an inability to prevent redeposition on clothes. The zeolites cannot sequester magnesium and need an auxiliary builder; the silicates lack general calcium binding capacity; the citrates are much weaker sequestering agents than STPP.

Arm & Hammer laundry detergent is based on sodium carbonate as the builder because it is an effective material and because Church & Dwight has long worked with bicarbonates and carbonates.

Our Arm & Hammer Washing Soda is a hydrated sodium carbonate and also has been used for laundry purposes since the turn of the century. It was a natural starting material for us.

Sodium carbonate has good alkalinity needed to boost cleaning; it removes calcium and magnesium from the water so the surfactants can work better by precipitating them from solution; it is an economical raw material readily available in bulk; and it lends itself to blending with other ingredients to afford an acceptable finished consumer product.

Our carbonate-based detergent has been on the market for about 10 years and is perceived by many consumers as an effective laundry detergent, especially in the softer water areas and for greasy types of soils.

In fact, in an attitude and usage study conducted among a national probability sample of 3,200 laundry detergent users, it was found that satisfaction with cleaning for Arm & Hammer laundry detergent was equal with other major brands.

I'd like to turn now to the health and environmental effects of carbonates as used in laundry detergents.

Two surveys have been prepared for the FDA in its review of the GRAS, "generally recognized as safe," status of carbonates as food additives. They have summarized the biological effects of the various carbonates and bicarbonates.

The first of these is a document compiled by Informatics, Inc., Rockville, Md., under contract from the Food and Drug Administration. The second of these reviews was prepared for the FDA in 1975 by the Life Sciences Research Office of the Federation of American Societies for Experimental Biology.

A summary of these reports shows that teratogenic studies in mice and in rats indicate no birth defects from ingestion of sodium carbonate at any of the levels fed.

Neither potassium carbonate nor sodium bicarbonate were mutagenic in in vitro assays with *Saccharomyces* and *Salmonella* in the Ames test.

The oral LD50 in rats for sodium carbonate monohydrate has been estimated at 2,800 milligrams per kilo of body weight, which that of sodium bicarbonate ranges from 4,800 to 6,000 milligrams per kilo of body weight. Although sodium carbonate is more toxic by oral ingestion, laundry detergents containing it are appropriately labeled under the Federal Hazardous Substances Act, and no fatalities have resulted from ingestion of such a detergent.

While the range of available studies in mammalian species including man is quite limited, the available information about the effects of carbonates in man are derived primarily from many years of treatment of ulcer patients with extremely high doses. For example, administration of sodium bicarbonate daily for 3 weeks to 33 patients at the rate of 2,300 milligrams per kilo—and if we take an average adult as 70 kilos, this would be close to 161,000 milligrams or almost 6 ounces daily—resulted in marked alkalosis but no other adverse effects. Increased urine excretion with no kidney damage removed the excess.

In another study one individual received 32,000 grams or 70 pounds of bicarb over a period of 20 months with no effects.

Treatment of gastric and peptic ulcers with high levels of carbonates and bicarbonates indicates no adverse effects other than a transient change in acid-base ratio. Accordingly, the FDA has approved sodium bicarbonate, aluminum carbonate, magnesium carbonate, calcium carbonate, sodium carbonate, potassium carbonate, bismuth carbonate, and dihydroxy aluminum sodium carbonate as over-the-counter antacid ingredients.

The carbonates and bicarbonates are readily metabolized and excreted either as respiratory carbon dioxide or through the kidneys.

The average intake of carbonates and bicarbonates from food has been estimated in this GRAS review study at about 1,100 milligrams per day.

The conclusion of the Select Committee on GRAS Substances states:

There is no evidence in the available information on calcium carbonate, potassium carbonate, potassium bicarbonate, sodium carbonate, sodium bicarbonate, or sodium sesquicarbonate that demonstrates or suggests reasonable grounds to suspect a hazard to the public when used at levels that are now current or that might reasonably be expected in the future.

Concerning environmental considerations, it is well known that carbonates are ubiquitous in nature, occurring in such rocks as calcite, dolomite, limestone, and marble. Carbon dioxide from the air dissolves in surface waters to form carbonic acid which can react with various minerals and rocks to produce carbonates and bicarbonates in solution, the exact nature of the species depending upon the pH of the water. Therefore, carbonates are natural to our environment, both land and water.

The effect of additional sodium carbonate from laundry detergents to various aspects of the environment has been either calculated, determined experimentally in the laboratory, or studied in the field. A brief summary of the data indicates that the contribution of sodium carbonate from laundry detergents to surface waters

can be calculated and would come out roughly at 10 milligrams per liter.

A brief listing of the carbonate levels in drinking waters in representative cities in several areas of the country indicates that it ranges from a low of 25 milligrams per liter to 275 milligrams per liter. Therefore, the 0.093 milligram per liter carbonate from laundry detergents would obviously contribute less than 1 percent of the naturally occurring load.

In raw sewage, the net increase in alkalinity due to the addition of sodium carbonate and compensating for the removal of the phosphate is only about 2.5 milligrams per liter, which is minimal.

It has been observed that sewage sludge settles faster when calcium carbonate—that is, limestone—is added to the activated sludge. The addition of sodium carbonate as well as sodium bicarbonate also increases settling rates and compactness without adding additional weight and volume.

Assuming that all the soluble sodium carbonate were converted to insoluble calcium carbonate in the treatment plant, a most unlikely event, the maximum solids contribution to the wet sewage sludge can be calculated to be an increase of about 0.3 of a percent in weight and 0.1 percent in volume.

Field studies conducted at the Canadian Forces Station in Gloucester, with four different detergent builders, showed that carbonates had minimal effects on influent and effluent sewage pH and alkalinity, and no adverse effects on the biological treatment process of the sewage treatment plant.

Aquatic toxicity has been determined for sodium bicarbonate and sodium carbonate on a large number of fish, water insects, and diatoms. For sodium carbonate, the more toxic of the two, the lethal concentration ranges from a low of 68 milligrams per liter for the Chinook salmon to a no-effect concentration of 552 milligrams per liter for the water flea. The concentration of carbonate from detergents in raw sewage, about 10 milligrams per liter, is well below the concentrations shown to have any adverse effects on the aquatic life, and the dilution would immediately decrease the concentration even further.

Sodium carbonate has shown no toxicity effects up to 200 milligrams per liter against three species of algae, nor is it expected to stimulate growth based on extensive studies of the effects of organic and inorganic carbon on algae over the past 10 years.

In conclusion, I believe the above information indicates that sodium carbonate poses no discernible hazard to the environment at the concentrations resulting from its use as a laundry detergent builder.

Thank you.

Mr. MAGUIRE. Thank you, Dr. Lehne. The tables attached to your prepared statement will be made part of the hearing record.

[The tables referred to follow:]

TABLE 1

RAW SEWAGE LEVELS RESULTING FROM THE USE OF SODIUM CARBONATE IN LAUNDRY DETERGENTS

I. BasesU.S. Laundry Detergent Market Volume : 3×10^9 lb./yr. (1974)Product Composition: 20% Na_2CO_3

U.S. Population : 211,381,000 (July 1, 1974)

U.S. Sewage Flow : 100 gal/capita/day

U.S. Sewage Effluent Dilution (Avg.) = 1:100

II. Calculation - Raw Sewage

$$3 \times 10^9 \frac{\text{lb. detergent}}{\text{year}} \times 0.20 \frac{\text{lb Na}_2\text{CO}_3}{\text{lb detergent}} \times 454 \frac{\text{gm}}{\text{lb.}} \times 10^3 \frac{\text{mg}}{\text{gm}} = 9.3 \text{ mg/l}$$

$$211 \times 10^6 \text{ capita} \times 100 \text{ gal/capita/day} \times 3.79 \text{ liter/gal} \times 365 \text{ days/yr}$$

III. Calculation - Surface Waters

$$9.3 \text{ mg/l} \times \frac{1}{100} = 0.093 \text{ mg/L}$$

TABLE 2

CO₃⁼⁼ AND HCO₃⁼⁼ CONCENTRATIONS IN RAW DRINKING WATER SUPPLIES

	Great Lakes			Eastern Coast			Mid-West	
	CO ₃ ⁼⁼	HCO ₃ ⁼⁼		CO ₃ ⁼⁼	HCO ₃ ⁼⁼		CO ₃ ⁼⁼	HCO ₃ ⁼⁼
	mg/l			mg/l			mg/l	
Milwaukee, Wisc.	0	134	Newark, N.J.	0	23	Topeka, Kan.	0	322
Chicago, Ill.	1	132	Richmond, Va.	0	41	Des Moines, Iowa	0	340
Detroit, Mich.	1	95	Charlotte, N.C.	0	20	Kansas City, Mo.	0	198
Buffalo, N.Y.	0	111	Atlanta, Ga.	0	15	Omaha, Neb.	0	238
Avg.		118	Avg.		25	Avg.		275

Mr. Krumrei, do you or Mr. Pepper wish to proceed?
 Mr. KRUMREI. May I yield to Mr. Pepper first, please?

TESTIMONY OF JOHN E. PEPPER, AND WILLIAM C. KRUMREI

Mr. PEPPER. Mr. Maguire, gentlemen, good morning. My name is John Pepper, vice president of the Procter & Gamble Co. With me this morning in addition to Mr. William Krumrei and who have been sworn in are Mr. Doug Cowan, who is in charge of our Product Development Group in the Packaged Soap and Detergent Division, and Mr. Robert Winters, who is manager of Professional and Regulatory Services for the same division. Also with us is Dr. Leon Golberg, president of the Chemical Industry Institute of Toxicology.

We believe that what is at issue here today is whether American consumers will be permitted to get the value which we believe the use of NTA in detergent formulations can provide for millions of families.

Our testing over almost 20 years has established that NTA can be of real value to consumers by improving the cleaning performance of their detergents and that it can be safely used in these products.

As you well know, American consumers these days are facing a variety of problems day in and day out. They face inflation and rising energy costs, and they face the problem of getting the laundry done right. Now laundry isn't the biggest problem in the world, but it does bear on their battle with inflation and rising energy costs. These days the typical wash contains a high level of synthetic blends in clothes which are just inherently harder to get clean. The cost of hot water, of course, continues to escalate as energy costs grow.

With the more effective detergent formulations that NTA would permit, we believe that many consumers could reduce their energy bills by using less hot water and still get excellent performance. Many consumers could also reduce the use of various laundry additives which would be less necessary if the detergent they were using contained NTA.

In particular, consumers in the 20 percent of the United States where phosphates are regulated by law and where present detergent formulations are less effective would benefit from NTA-containing detergent formulations.

Let me make it clear that we are not using NTA in the United States today and we haven't since 1971. We will continue to work to provide the best products we are humanly capable of making with or without NTA. However, we do think it is too bad and unreasonable not to be able to use an ingredient that in our best judgment and based on all the testing available is safe when it could importantly improve the value which many consumers in the United States receive from their laundry detergent.

We hope that this committee hearing can help convince the public of the safety of NTA based on the testimony we present today.

The consumers in Canada and several other countries in Europe already have the potential benefits offered by NTA formulas. We

see no good reason why U.S. consumers should not be granted the same benefits.

Before I introduce Mr. Krumrei, who will talk to what is obviously the basic issue that is being talked about today, safety, I would just like to make one personal plea to the committee. Recognizing that you are extremely busy and that your staffs are extremely busy, I would simply like to urge that you review as closely as you can all of the written material that has been submitted on this very complex subject, and also the letters which Mr. Dannemeyer suggested come in, so that the judgments that you do reach on this subject will have been based on a full consideration of this complex subject and not just the testimony which, trying as hard as we can, we and others will present today.

Mr. MAGUIRE. Mr. Krumrei?

Mr. KRUMREI. Mr. Chairman and members of the subcommittee, I am William C. Krumrei, senior director of Research and Development, Procter & Gamble Co. I plan to present a summary of our total written testimony [see p. 74], to which Mr. Pepper has already referred. With your permission, Mr. Chairman, we will submit the complete text for the record along with pertinent key information which we already submitted which we believe will help this subcommittee understand the safety of NTA.

In your discussion with Mr. Martin this morning, Mr. Chairman, you raised the question of the use of laundry detergents for handwashing and hand laundry. I would also like to request your permission to submit for the record a letter from me to Dr. Muir asking for clarification of EPA's letter to me and also his response to me, which in part I quote:

We have not conducted thorough risk assessment for products other than conventional laundry detergents with their customary uses of machine laundry, hand laundry, and occasional hand dishwashing.

If I may, I would like to submit that, sir.

Mr. MAGUIRE. Without objection, that will be included in the record following your written statement [see p. 94].

Mr. KRUMREI. Thank you, Mr. Chairman.

Mr. MAGUIRE. I should ask you, though, inasmuch as we are going to include it in the record, whether the fact that EPA included some strictures with respect to the use of NTA in foods, shampoos, and dishwashing was a surprise to you at the time that they issued their report.

Mr. KRUMREI. Yes, it was a surprise to us because we expected that we had given enough information to EPA to show that dermal exposure—that is, hand exposure and so forth—was satisfactory. They also had concluded that apparently, since it was in their risk assessment for hand laundry and hand dishwashing with laundry detergents.

Based on Mr. Muir's comment, he said:

Given the toxicological properties of NTA—

And I am continuing to quote—

And the limited scope of our risk assessment, we felt it prudent to recommend that NTA not be marketed in other products specifically designed for food and shampoo use and other prolonged and frequent dermal or oral exposure without our having had the opportunity to conduct a full assessment of any data supporting such use before marketing.

They were completely in accord with what you are saying, Mr. Chairman.

Mr. MAGUIRE. In effect, they set aside your suggestion in the letter that has just been included in the record. You wrote to them—and I do not have the letter before me—

Mr. KRUMREI. It is in the public record because it was part of the whole EPA record.

Mr. MAGUIRE. Yes. I had it here earlier.

If I recall correctly, you felt it really should not cover those items.

Mr. KRUMREI. I was asking for clarification as to whether they had considered hand laundry and hand dishwashing. They, in turn, indicated, yes, they had. That was part of their risk assessment for a laundry detergent.

I will be glad to have one of the staff give it to you, sir.

Mr. MAGUIRE. Would you like to continue with your testimony?

Mr. KRUMREI. Thank you.

In the brief time we had it was impossible to assemble all of the printed publications on this material, but I have with me a computer printout. This is it in front of me. It lists more than 1,100 research citations from Chemical Abstracts, which includes those covering the human and environmental safety of this material as well. I would also like to submit this for the record, Mr. Chairman.

Mr. MAGUIRE. That will be made part of the subcommittee's file.

Mr. KRUMREI. Thank you, sir.

The point of all this, Mr. Chairman, in talking about all of this data, is that it is my belief that from a human and environmental standpoint more is probably known about NTA than any other chemical used in commerce.

NTA was used broadly in some detergent brands in the United States in the late 1960's. In December 1970 the major detergent manufacturers voluntarily discontinued the use of NTA in laundry detergents at the request of the Surgeon General and the EPA Administrator. This request was based on preliminary results from tests conducted by the U.S. National Institute of Environmental Health Sciences.

Retesting by this group and others later showed these preliminary results to be erroneous. This clarification was made about a year later by the Surgeon General who indicated that he no longer had concern about the safety issues raised by the preliminary information. Shortly after the issuance of this report, however, HEW requested that the voluntary agreement against the use of this material be continued until further chronic studies could be completed.

In contrast, the Canadian Government in early 1971 reaffirmed the suitability of NTA for use in detergents, and it has been used in that country by most manufacturers since that time. Indeed, NTA has also been approved for and used in detergents in Sweden since 1968 and in Finland since 1970. It is on the approved list of detergent ingredients in Venezuela and Peru, and in January 1980 the Government of the Netherlands also approved its use.

Incidentally, the use of this material in the United States has continued in many other applications without interruption. For example, the FDA has approved the use of NTA as a boiler water

treatment additive for food plants. Because of this and other uses in the United States, environmental monitoring has identified a low background level currently existing in three widely separated U.S. waters, including the Potomac River.

The Procter & Gamble Co. believes that we are solely responsible for the human and environmental safety of our products. Neither performance gain nor cost advantage permits us to even consider the marketing of a product which we feel could not be safely handled by our employees and by the consumers.

Mr. MAGUIRE. Mr. Krumrei, excuse me. When you use the word "solely" at that point, do you mean that we should not be concerned about the environment?

Mr. KRUMREI. No, sir. However, we feel that we ultimately are the ones that are responsible for the marketing of our product.

Mr. MAGUIRE. In effect, you are saying you assume full responsibility rather than sole responsibility?

Mr. KRUMREI. That is a better way of saying it, Mr. Chairman.

Mr. MAGUIRE. Thank you.

Mr. KRUMREI. You are quite welcome.

With NTA no such tradeoff is even at issue. The scientific data base supporting our conclusions on the safety of NTA is exhaustive. We take particular pride in the fact that this data base has been subjected to peer review not only within our company but by other scientists and governmental experts in the United States and several other countries.

The basic reasons why we believe NTA is safe from an environmental and human standpoint are, and I will tick these off very quickly:

It is a simple, low molecular weight compound of known structure;

It is over 99 percent pure as used commercially;

It is easily biodegradable, both as a sodium salt and as a complex with metals;

It does not accumulate in fish;

It has extremely low toxicity to fish, algae, or other aquatic species;

It exhibits no buildup in surface or ground waters. This has been exhibited in Canada where it has been used in both soft and hard waters.

It does not adversely affect sewage treatment;

It does not adversely affect drinking water treatment;

It does not mobilize heavy metals;

NTA has a low oral toxicity;

NTA has low irritancy to skin, eyes, or respiratory tract;

NTA is not a skin sensitizer;

NTA is poorly absorbed by humans;

NTA is not changed by the body and it passes unaltered through the body via feces and urine;

NTA is not a mutagen;

NTA is not a teratogen, either alone or combined with heavy metals;

NTA exhibits no cocarcinogenic properties; and

NTA exhibits urinary tract toxicity only at massive levels in the diet, but exhibits a "no-effect" level for this cancer in rodents, a

level below which a risk of cancer does not exist. This conclusion is based on our research which demonstrates that NTA's chelating properties—its ability to tie up calcium and zinc—produce an imbalance in metal distribution only at very high levels in the diet.

In 1977, the National Cancer Institute published a bioassay study which raised a question regarding the safety of NTA. This study showed that at very high dose levels there was cancer formed in the urinary tract of rodents whereas the remaining lower levels showed no such cancers nor any urinary tract toxicity. The summary of the NCI study pointed out, and I quote:

Since NTA and trisodium NTA monohydrate are eliminated rapidly through the kidneys, lesions of the urinary tract which arise as a result of the administration of the compounds may be due to a local effect which can be brought about only by high concentrations.

These comments in the National Cancer Institute report further encouraged our ongoing extensive research on the relationships between the urinary tract toxicity and cancer at high dose levels in the rodent, and the absence of cancer and any observable urinary tract toxicity at low doses. The results of this research led to our discussions of about a year and a half ago with NCI. Essentially all of this work has already been published in the scientific literature and the remainder has been submitted for publication. All of this information has been shared with NCI and EPA scientists.

The significance of our finding is that cancer with NTA has never been observed without abnormalities in the accompanying tissues. The cancer response at the massive doses employed in the NCI study results from a dose dependent NTA-caused imbalance in the handling of calcium and zinc by the test animals. In the absence of enough NTA to create this imbalance, neither the urinary tract toxicity nor the cancer effect can occur.

The highest no-effect level is hundreds of thousands of times higher than human exposure levels expected via drinking water from the use of NTA in laundry detergents. This expected human exposure level has been determined by the Canadian Government, as well as by Procter & Gamble, and it is shown to be extremely small. In fact, a human consumption of over 80,000 gallons per day of water containing that NTA level for an entire lifetime would be necessary to reach the highest no-effect level in animals.

I would like to dramatize that just a little bit, Mr. Chairman. Mr. MAGUIRE. I thought that was probably why you had included it.

Mr. KRUMREI. You are quite right.

The amount of NTA in this vial [indicating bottle] represents the amount of NTA that would be ingested by a human over an entire 75 years of a human's life at the level of NTA in Canadian waters.

Mr. MAGUIRE. What is the significance of that?

Mr. KRUMREI. Excuse me one more moment, please.

The amount in this vial [indicating another bottle] represents the amount that a human would have to take every day of his life for 75 years to reach the toxic effect levels seen by NCI.

We believe this is a fairly dramatic difference, sir.

Mr. MAGUIRE. It depends on what is in the bottles.

Mr. KRUMREI. This is NTA.

Mr. MAGUIRE. If you had dioxin, for example—

Mr. KRUMREI. This is not dioxin, sir. This is NTA.

Mr. MAGUIRE. All I am seeking to suggest is the demonstration with the bottles does not really help us very much when we look at what the scientific questions are about carcinogens.

Mr. KRUMREI. Yes, sir, but this does help dramatize for the lay person, I believe, a little bit about what 2.8 ppb for a 75-year lifetime would mean versus what the rat was fed in order to get the cancer that was incurred.

This highly complex subject is covered more thoroughly in our written testimony. From all of these data, we conclude that NTA cannot form cancer at the levels which would be encountered by humans if NTA were to be used in all detergents in the United States. This same conclusion that NTA does not cause cancer at these low levels was reached in January 1980 by the Government of the Netherlands after careful examination of all data by their scientists.

One other point needs to be made. The National Toxicology Program Subcommittee, to which Dr. Rall referred, which reviewed the safety of NTA for the National Toxicology Program Executive Committee, suggested that NTA might act as a cocarcinogen. The suggestion remained in spite of the fact that an existing but pertinent unpublished NCI study was called to the attention of that subcommittee. In that portion of the study containing NTA plus nitrosamines, a known animal cancer-causing agent, the data showed that there was no enhancement of the cancer-causing activity of the nitrosamines; rather, there was actually a protective effect by NTA against cancer in the urinary tract and stomach. Therefore, we believe that this clearly shows by NCI's own data that NTA does not enhance the cancer-causing effect of known cancer agents.

Mr. MAGUIRE. What about other known cancer agents, other than nitrosamines?

Mr. KRUMREI. Nitrosamines are those they studied, sir.

Mr. MAGUIRE. Right, but they did not study the others, did they?

Mr. KRUMREI. No. They studied a total of about—I think I have it here—something on the order of a dozen compounds.

Mr. MAGUIRE. There are many more than that which are known to be carcinogenic?

Mr. KRUMREI. There are roughly 25 known human carcinogens, yes.

Mr. MAGUIRE. There are many more that are suspected.

Mr. KRUMREI. There are many other animal carcinogens, that is correct.

Mr. MAGUIRE. Therefore, it would be very difficult to conclude that NTA or any other suspect chemical agent could be shown not to be a cocarcinogen on the basis of a test of that compound with one or five or however many compounds you wanted to test it with as long as they were relatively few and did not reflect the whole universe?

Mr. KRUMREI. It is my understanding they chose these because they were probably among the most potent that they could think of and the ones that contained nitrogen, which has been alleged to have been a problem in the past with NTA.

Mr. MAGUIRE. I just wanted to point out that the conclusion does not seem to follow from the premise.

Please proceed.

Mr. KRUMREI. This specific NCI study was conducted by Stanford Research Institute under the sponsorship of NCI and was completed in 1976. The study was designed as an additive risk bioassay and included both high and low levels of NTA alone as well as NTA plus three known carcinogen nitrosamines. Only the NTA control portion of the test which has been the subject of so much discussion, known as the bioassay study, was published. The remaining portions of this study, which in addition to NTA and nitrosamines included a number of other ingredients such as aflatoxin and dieldrin, has to date been unpublished.

As a result of all of these new data which have become available over the last several years, we believe that every serious concern that has been raised about NTA has been addressed and favorably resolved. This position is shared by the scientists who have reviewed this matter for the Governments of Canada, the Netherlands, Sweden, Finland, as well as by the Science Advisory Board of the Canadian-United States International Joint Commission for the Great Lakes, all of whom have approved the use of NTA in detergents.

With regard to your comment to Dr. Spacie before, the actual quote from the report of the IJC was that, "There is no reasonable cause for the restriction of the use of NTA," and that is why I took the liberty of saying that was an approval.

Our interest in using NTA is based on the belief that it can make a worthwhile contribution to the cleaning effectiveness of laundry detergents and that it is safe. As a practical matter, however, NTA will only be used in U.S. detergents if consumers are convinced of its safety.

We hope that as these data become available to competent, objective scientists, the true picture of NTA's safety can be ultimately conveyed to the U.S. public. Then the advantages that this ingredient has to offer can be realized in U.S. laundry detergents. We hope that this subcommittee hearing will contribute to that objective.

Thank you, Mr. Chairman.

[Testimony resumes on p. 96].

[Mr. Pepper's and Mr. Krumrei's prepared statement and correspondence referred to follows:]

WRITTEN TESTIMONY OF
THE PROCTER & GAMBLE COMPANY
PRESENTED BY
JOHN E. PEPPER AND WILLIAM C. KRUMREI
BEFORE THE
SUBCOMMITTEE ON INVESTIGATIONS & OVERSIGHT
OF THE
HOUSE COMMITTEE ON INTERSTATE & FOREIGN COMMERCE
June 26, 1980

MR. PEPPER

Good morning, Mr. Chairman and Members of the Subcommittee. I am John Pepper, Group Vice President of The Procter & Gamble Company. With me this morning is Mr. William C. Krumrei, Senior Director, Research and Development, for Procter & Gamble. Mr. Krumrei will address the safety aspects of WTA's use in detergent products.

Also present with me are Dr. Robert E. Winters, Manager of Professional and Regulatory Services for the Company's Packaged Soap and Detergent Division, and Dr. Leon Gelberg, President of the Chemical Industry Institute of Toxicology.

Procter and Gamble has built its business on the principles of providing consumers with products which are needed, effective and safe.

We are here today to present testimony about nitrilotriacetate (NTA) which we have studied and tested in laundry detergents for almost 20 years. NTA has been used in detergents in Canada, Sweden, and Finland for about 10 years, but not in the U.S. since 1971. It is an ingredient about which a tremendous amount of scientific information is known.

It was impossible to assemble all of the printed publications on this material in this brief time, but we have with us a computer print-out which lists the over 1100 research citations in Chemical Abstracts which includes those covering the human and environmental safety of this material. This will be submitted for the record.

The key conclusion to be drawn from all of this information is that NTA is safe and that it does not present a cancer risk at the levels to which humans would be exposed if this material were to be used in detergents. It is our belief that from a human and environmental standpoint, more is probably known about NTA than any other chemical in commerce.

Our testing over the years has established that NTA can be of value to U.S. consumers by improving the cleaning performance of laundry detergents. It does this by tying up water hardness materials which impede the ability of other detergent ingredients to do their job of removing dirt. Consumers are clearly telling us that there is a real need for improving cleaning in detergents. The challenge to getting clothes clean today is greater than at any time in recent history. Some of the reasons for this are the trend to the use of cooler wash water as an energy-saving measure, an increase in synthetic fiber blends in clothes which are simply harder to get clean, and the fact that in approximately 20 percent of the U.S. households, phosphates are regulated by law. Today, in those areas we use alternative materials, including sodium carbonate and sodium aluminosilicate, which while providing cleaning benefits are less effective than either phosphate or NTA.

Despite the benefits which NTA would offer consumers, we are not using this ingredient in our U.S. detergents. The reason has been unjustified concerns about

WTA's safety. Mr. Krumrei will now explain the basis for our conviction in WTA's safety.

MR. KRUMREI

Chairman Eckhardt's letter of June 19 identified three areas which we shall address in this testimony:

- I. the rationale for the initial development of WTA;
- II. the current regional phosphate bans and Procter & Gamble's marketing of non-phosphate substitutes in such areas; and
- III. Procter & Gamble's request to the EPA and HCL for a re-look at WTA in the late 1970's and the reasons for such a request.

Our initial and continuing interest in WTA as a detergent ingredient has been based on two simple facts. First, we are convinced that it is safe. Second, we know that it can be of value to U.S. consumers -- by improving the cleaning performance of laundry detergents.

Let me elaborate briefly on these two points:

- I. WTA, which is an acronym for sodium nitrilotriacetate, is, as Mr. Pepper has pointed out, a detergent builder. As I noted in 1970 during my testimony before the Senate Subcommittee on Air and Water Pollution of the Committee on Public Works, Procter & Gamble has tested literally hundreds of alternative materials and out of all those tests we have found only one material which would serve as an acceptable builder in detergents at that time. While it is not a fully satisfactory replacement for phosphate, WTA is superior to other currently available alternative materials. I further stated "Behind all of our work is a very strong motivation to continue to produce products with the cleaning levels that our customers have chosen and demanded of our products."

in essence, we feel an obligation to provide housewives in this country with the best possible cleaning product.

We know from all our testing and 10 years of actual usage of this ingredient in Canada that NTA can make a worthwhile contribution to improved cleaning. This improvement is particularly needed in the approximately 20% of the households in the U.S. where phosphates are regulated by law. Currently, state level legislation prohibits or otherwise limits the use of phosphates as a laundry detergent builder in the following areas:

- Indiana
- Florida
- New York
- Minnesota
- Michigan
- Connecticut
- Maine
- Wisconsin
- Vermont.

In addition, local county or municipal phosphate legislation is in effect in approximately 40 locations. Today, in these state and local areas, we use alternative builders including sodium carbonate and sodium aluminosilicate, which, while providing cleaning benefits, are significantly less effective than either phosphate or NTA.

2. Despite the benefits which we believe this ingredient would offer consumers, NTA has not been used in detergents in the U.S. during the past 10 years. The

reason has been unjustified concerns about its safety. I will address the balance of my remarks to this issue. At the onset, let me emphasize that the safety of our products is an integral part of our product development process.

No factor, whether it be performance or cost or whatever, would lead us to consider for a moment, marketing a product or ingredient which we felt consumers could not use safely in their homes or that our employees could not handle safely in our plants. This is true of any product or ingredient we market. What makes us particularly assured of NTA's safety is the breadth of the scientific work that has been done on it -- both by our Company and by outside scientific and governmental experts in the U.S. and elsewhere. I will now comment on the basis for our conviction in NTA's safety.

Introduction

On May 27 of this year the U.S. Environmental Protection Agency released the results of a risk assessment on the use of NTA in laundry detergents. A copy of the EPA's report is included with our supporting documents. This review of NTA, which included all of the available major studies, found that the projected levels of exposure from the use of this substance in laundry detergents were generally low and therefore the associated risks would also be low. The EPA indicated that it saw no reason to take regulatory action against the resumed production and use of NTA for laundry detergents.

Procter & Gamble has been, and remains, confident that NTA is safe for use in laundry detergents. NTA has been extensively studied in 20 years of comprehensive testing by industry, academia, and government. We ourselves have contributed almost

combinations of phosphate and NTA are attractive from a performance viewpoint. On the other hand, completely satisfactory performance cannot be obtained by complete replacement of phosphate with NTA.

The early use of NTA in laundry detergents in the late 60's was in combination with phosphate to produce a superior product not practically achievable by the use of phosphate alone.

History of Regulatory Status

At the present time, commercial use of NTA is not prohibited in any country in the world, including the U.S. NTA has been continuously and broadly used in detergents in Canada since 1970, in Sweden since 1968 and in Finland since 1970 with the approval of the respective governments. It is also on the approved list of detergent ingredients in Venezuela and Peru. In January, 1980 the government of The Netherlands approved its use. The major U.S. detergent manufacturers voluntarily discontinued the use of NTA in December, 1970 at the request of the Surgeon General -- a request incidentally shown later to have been based on preliminary and erroneous results. These preliminary studies, conducted by NIEHS, showed apparent enhancement of teratogenic effects of very high levels of NTA in combination with very high levels of toxic heavy metals (cadmium and mercury) in rats and mice. A joint Government/Industry Committee including the researchers who conducted the preliminary studies was formed to design experiments to address deficiencies in a repeat of the initial NIEHS work. Following completion of these definitive studies, NIEHS issued a report (September 8, 1971) which provided a comprehensive statistical analysis of the results. The report, entitled "Statistical Summary: Teratology of Oral Administration of NTA to Rats, NIEHS" stated "These studies indicate teratogenic and fetotoxic effects of mercury and cadmium although the addition of NTA does not appear to enhance their activity." This, then, refuted the conclusion

20 years of our own research on its safety. Included among our supporting documents are a number of reviews which address the pertinent safety publications, as well as a bibliography of more than 350 scientific papers on NTA safety.

Our position on NTA's safety is supported by the conclusions reached by qualified scientific experts in the Canadian Government, and also by the U.S. and Canadian International Joint Commission in 1977, and by The Netherlands government in January, 1980, after a thorough review on the safety of NTA. All of these reviews considered the NCI studies which were completed in 1976, and reported in 1977, and which are discussed later.

Background

NTA belongs to a family of chelating agents -- the aminocarboxylic acids. It was first synthesised 118 years ago but found little commercial application until 74 years later. In 1936, commercial production of NTA was begun for use in the textile industry in water softening and as a dye stabilizer. Due to its high cost, NTA's use was limited until 1960 when a new manufacturing process was developed by the Hampshire Chemical Corp. This new process reduced NTA's manufacturing cost and made high purity material available for other applications. The wide range of uses for high purity NTA included water softening, leather, textile and paper production, horticulture, food processing, agronomy, and applications in the photographic, electrical, rubber and plastics industries.

All of these uses and applications of NTA result from a single chemical property: its complexing reactions with metal ions in aqueous solutions. Especially significant is that NTA is an effective chelator of divalent metals such as calcium and magnesium. This property made it of interest as an ingredient in laundry detergents to counteract the adverse effects of calcium and magnesium on detergency. Phosphates also have this property to a different degree so that

drawn in December, 1970 based on the preliminary NIHS experiment which had resulted in the voluntary withdrawal of NTA at the request of the Surgeon General. Shortly after the issuance of this report, the U.S. Government requested that the voluntary agreement against the use of this material be continued until further chronic studies could be completed.

During the time since 1970, other industrial applications of NTA have continued without interruption in the U.S.A. Approximately 10 million pounds are used annually in the U.S. for such purposes as boiler water treatment, tannery and textile operations, and industrial cleaning. In fact, NTA is "cleared" as a boiler water additive for food plants by the U.S. FDA.

Because of this and other uses in the U.S., environmental monitoring has identified a low background level currently existing in three widely separated U.S. waters, including the Potomac River. A copy of our monitoring results for background environmental levels of NTA are included in our supporting documents.

In 1977, the International Joint Commission for the Great Lakes after a full review of NTA data by its Scientific Research Advisory Board (composed of U.S. and Canadian scientists), concluded, "On the basis of a health hazard, there is no reasonable cause for restricting the use of NTA as a replacement for phosphate in detergents in the Great Lakes Basin." A copy of the report to the Research Advisory Board by its Task Force on the Health Implications of NTA is included in our supporting documents.

Concurrently, a Task Force on the Ecological Effects of Non-Phosphate Detergent Builders reviewed the environmental aspects of NTA use. This Task Force consisting of scientists from government and academia, recommended, in 1978, that "NTA should not be prohibited from use as a detergent builder." This recommendation was accompanied by suggestions on nine areas where additional information would be

considered helpful. These comments also appear in the EPA assessment document. A copy of the Task Force Report and Procter & Gamble's discussion of the nine suggestions as they appear in the EPA risk assessment are also included among our supporting documents.

In January of 1980, The Netherlands formally concluded that there were no safety objections to the gradual introduction of NTA in detergents. The Netherlands' decision was preceded by an in-depth review of the up-to-date available data by a Consultative Group for the Reduction of Phosphate. This is discussed in more detail later in our testimony.

Discussion of P&G Position on NTA Safety

An enormous base of published information exists in the scientific literature for NTA. Reviews of these data are included amongst our supporting documents. These include, most notably, the reports of the Task Force of the International Joint Commission on health effects and ecological effects of NTA, the Report of the Consultative Group for the Reduction of Phosphate (The Netherlands), Procter & Gamble's summary booklet entitled Environmental Safety of NTA, a 1972 review by Arthur D. Little, Inc., and a number of recent scientific papers which address the significance of the no-effect level for urinary tract toxicity and cancer in the rodent.

The important facts about NTA may be summarized as follows:

Chemically,

- * NTA is a simple low molecular weight compound of known structure;
- * It is 99%+ pure as used commercially;
- * It is a chelating agent for divalent metals including calcium and magnesium.

Environmentally, NTA

- * Is easily biodegraded, both as a sodium salt and as a complex with divalent metals;
- * Does not accumulate in fish;
- * Has extremely low toxicity to fish, algae, or other aquatic species;
- * Exhibits no build-up in surface or ground waters;
- * Does not adversely affect sewage treatment;
- * Does not adversely affect drinking water treatment;
- * And it does not adversely mobilize heavy metals in sewage treatment or in surface waters or drinking waters.

Toxicologically, NTA

- * Has a low oral toxicity;
- * Has low irritancy to skin, eyes, or respiratory tract;
- * Is not a skin sensitizer, it is poorly absorbed by humans;
- * Is not metabolized;
- * Is excreted unchanged in the feces and urine;
- * Is not a mutagen -- the NTP report concluded that "the mutagenicity data on NTA show no production of gene mutations or chromosome aberrations that would be of concern to an exposed human population" -- and that "there is no evidence that NTA is a mutagen".;
- * Is not a teratogen; either alone or combined with cadmium or mercury;
- * Exhibits no co-carcinogenic properties;
- * Exhibits effects only at massive levels in the diet where its chelating properties affect the metabolism of zinc or calcium in the rodent producing urinary tract toxicity including cancer; and

Exhibits a threshold or "no-effect" level for cancer in rodents and at doses below the threshold level which is still a highly exaggerated level compared to human exposure, NTA is not a carcinogen nor does it produce any observable urinary tract toxicity.

The environmental aspects of NTA have not only been studied extensively in the laboratory but also extensively in the real world environment. Extensive monitoring data have been collected by the Canadian Government (and by Procter & Gamble) over many years.

A Canadian government report issued on NTA in the environment (D. H. Matheson, Nitrilotriacetic Acid (NTA) in the Canadian Environment. Inland Waters Directorate, Water Quality Br., Environment Canada Sci. Ser. #74, 1977) stated:

"The results of the national monitoring program are:

1. NTA has not accumulated in surface waters as a result of its expanded use in Canada. Rapid biodegradation takes place in the common aerobic wastewater treatment processes and continued in the receiving waters.
2. The nation-wide survey of municipal drinking waters, which has now extended over four years, shows relatively few cases where NTA occurs above the detection limits. Where higher values exist the raw water is polluted with wastewater containing NTA and is abstracted for use before sufficient dilution and degradation can take place.
3. In groundwaters, degradation under the prevailing anaerobic conditions is slower and higher levels of NTA are observed in waters from aquifers which are grossly polluted. This problem occurs locally where a shallow aquifer received drainage from septic tanks and soakage pits.

4. Municipal water supplies derived from groundwater show little evidence of pollution by NTA."

The only effect which warrants further discussion is that on long term toxicity of NTA mentioned above. A number of rodent studies have been conducted over the past 10 years. Perhaps the most informative, a two part study, conducted under the sponsorship of the National Cancer Institute, and completed by 1976, is particularly notable and deserves comment.

Firstly, an additive risk bioassay was conducted by NCI at Stanford Research Institute, which was designed to study possible cancer enhancement effects of NTA with three known, potent, animal cancer-causing nitrosamines. Examination of the raw data obtained from NCI indicates that NTA does not exhibit a co-carcinogenic action.

In fact, the data show that NTA exerted a protective effect, i.e., it reduced the incidence of tumors caused by the known, potent carcinogens used in the test. However, these data have never been published despite the obvious relevance and importance of these results.

Secondly, a carcinogenicity study conducted with NTA by NCI included extremely high doses which were above the maximum tolerated dose as defined by NCI's own criteria. These high dose levels produced urinary tract toxicity and cancer in rodents while lower doses produced neither cancer nor urinary tract toxicity. The Discussion Section of the report is of particular interest. The following comments were included regarding the dose response relationships which were evident in these studies: "In all cases there was a rapid drop from the number of tumors observed at high doses to those at lower doses. This finding is consistent with that of Nixon, et al. who reported an absence of tumors in rats receiving 5000 ppm (=0.5%)

$\text{Na}_3\text{NTA}\cdot\text{H}_2\text{O}$ in the diet for two years." The Nixon study was completed internally by Procter & Gamble in the early 70's. The NCI report also points out: "Since NTA and $\text{Na}_3\text{NTA}\cdot\text{H}_2\text{O}$ are eliminated rapidly through the kidneys, lesions of the urinary tract which arise as a result of the administration of the compounds may be due to a local effect which can be brought about only by high concentrations." The critical phrase is "which can be brought about only by high concentrations" because, as discussed later, it is significant in the assessment of the biological properties and safety of this material.

The results of the NCI studies at the low doses are consistent with findings of the study conducted in-house by Procter & Gamble, and also those conducted by Lijinsky whose published findings reported no significant incidence of cancer. A copy of this paper is included amongst the supporting documents.

A consideration of the total evidence on NTA, indicating the lack of mutagenic properties together with the conclusions of the NCI study encouraged our ongoing research program. The objectives of the program were to study the relationship between the urinary tract toxicity and cancer observed only at high dose levels in the rodent and, more importantly, the absence of cancer and any observable urinary tract toxicity at low doses. Our more recent research (by Dr. R. L. Anderson) in this area has produced very significant findings which further reaffirm our earlier assessment of NTA's safety. It was these findings, the culmination of nearly four years of research which led to Procter & Gamble's latest interactions with NCI. Most of this work has already been published in the scientific literature -- one paper has just been submitted for publication. All have been shared with the NCI and the EPA scientists.

In essence, we have confirmed NCI's comment that "lesions of the urinary tract which arise as a result of the administration of the compounds may be due to a local

effect which can be brought about only at high concentrations." A number of our submitted documents cover research done in this regard. We believe our data is an important contribution to the understanding of the high dose effects of certain types of materials, especially chelators, when fed at massive doses to rodents.

The significance of our findings is that urinary tract cancer has never been observed in the rodent in the absence of other overt urinary tract toxicities. The carcinogenic response at the massive doses employed in the WCI study results from a dose dependent WTA-mediated metabolic imbalance on the disposition of calcium and zinc in the test animals. This occurs only at the extremely high levels.

For perspective as to the degree of exaggeration in these studies, a human could drink more than 80,000 gallons of water (containing the mean level of WTA in Canadian drinking water) each day for a lifetime and still remain below the no effect dose in rodents. To reach the level which produced cancer in the rodent it would require a daily consumption of approximately five million gallons of water for a lifetime (70-75 years).

In the absence of enough WTA to create this systemic imbalance neither the urinary tract toxicity nor the carcinogenic effect is seen. Obviously, no metal imbalance will be seen in humans at expected exposure levels which are approximately one hundred thousand times below the "no-effect" dose.

It is important that we not confuse this situation on WTA with direct chemical carcinogens which are also mutagens, i.e., they interact with DNA and are thus capable of causing a mutational event to initiate the carcinogenesis process. With such chemicals it is extremely difficult to obtain data to show a no-effect level for carcinogenesis. However, the situation with WTA is entirely different. It is not a mutagen and therefore not capable of causing a mutational event by direct

reaction with cellular DNA to initiate the carcinogenic process. WTA is therefore different from such direct acting carcinogens.

Our findings indicate that there is a threshold dose below which this biochemical overload in metal disposition in animals does not occur and therefore below which there is no observable urinary tract toxicity or cancer. Urinary tract toxicity including cancer is simply nonexistent at the low dose levels in the rodent, or at the more than 100,000 fold lower human exposure levels expected from the use of WTA in laundry detergents.

This view is shared by The Netherlands government and was reflected in their "report from the Consultative Group for the Reduction of Phosphate" in January, 1980. This group was composed of representatives from the Ministry of Health and Environmental Hygiene, the Ministry of Transport and Waterways, Ministry of Economic Affairs and the Federation of Dutch Soap Manufacturers. Interpretation of data and composition of advisory reports was provided by Prof. H. van Genderen (Institute for Veterinary Pharmacology and Toxicology, State University of Utrecht); the Hydromechanical Laboratory Delft; the Institute for Soil Fertility, Haren; the State Institute for the Purification of Wastewater, Lelystad; the State Institute for the Supply of Drinking Water, Voorburg; and the State Institute for Public Health, Bilthoven. This report contains the official conclusions of those respected scientists and agencies charged by the government with investigating the acceptability of various phosphate substitutes. They saw no objection from the point of view of the danger of cancer to the use of WTA in laundry detergents, because (1) the no-effect level for urinary tract toxicity is also the no-effect level for carcinogenesis, and (2) anticipated exposure levels resulting from use in detergents are well below these no-effect levels. The report clearly states that

the use of NTA would not be expected to increase the number of cancer cases. This conclusion, therefore, refers to a threshold exposure level of NTA below which no risk exists. The original Dutch version and a translation of the "Report from the Consultative Group for the Reduction of Phosphate, January, 1980", and a translation of the "Report to the Consultative Group on Phosphate Reduction Concerning the Carcinogenicity Risk Connected with the Introduction of Phosphate Substitutes" by Prof. H. van Genderen are included among supporting documents submitted to the Subcommittee.

One other point needs to be made. The National Toxicology Program Subcommittee which reviewed the safety of NTA for the National Toxicology Program Executive Committee suggested that NTA might act as a co-carcinogen. In spite of the fact that the previously noted existing but unpublished NCI study was called to the attention of that Subcommittee, this suggestion remained. The study was designed as an additive risk bioassay and as previously noted, included both high levels of NTA alone as well as NTA plus three nitrosamines. Only the NTA "control" portion of the test which has been the subject of so much discussion, the "bioassay study," was published. The remaining portions of this study, which in addition to NTA and nitrosamines, included a number of other ingredients such as aflatoxin and dieldrin, has not been published.

In that portion of the study containing NTA plus nitrosamines, the data showed there were no enhancement of the cancer-causing activity of the nitrosamines rather there was actually a protective effect by NTA against cancer in the urinary tract and stomach. Therefore, we believe that this clearly shows by NCI's own data that NTA does not enhance the cancer-causing effect of known cancer agents.

Summary of Procter & Gamble Position on NTA Safety

Based on the extensive chemical and toxicological data developed on NTA, most of which is published in the scientific literature, and briefly outlined above,

there is every reason to conclude that urinary tract toxicity including cancer observed in rodents only at exceedingly high doses, is a dose dependent effect and is non-existent at low doses. References to this literature are included on submission to the subcommittee. Next, the levels at which NTA no longer exhibits any observed urinary tract toxicity is also the levels at which it does not exhibit carcinogenesis in the rodent. It follows, therefore, that the maximum no-effect level can be used in the traditional way in comparison with the expected human exposure to determine exposure safety factors. On this basis, the maximum no-observable human effect dose level would be thousands of times higher than the predicted human exposure. This is a scientifically valid basis for concluding that it is safe to use NTA in laundry detergents.

To summarize, our interest in using NTA has been based on the belief that it can make a worthwhile contribution to the cleaning effectiveness of laundry detergents -- and that it is safe. To be clear, NTA alone is not a miracle ingredient but used in combination with other materials we believe it should provide a worthwhile improvement in cleaning performance, particularly in those areas of the country where phosphates are regulated by law. Since we feel the material is safe, we would like the option of being able to use it along with other builders such as phosphate and aluminosilicates and other cleaning ingredients. It benefits the consumer for the detergent industry to be able to use as broad a range of alternative materials as possible -- because this maximizes our ability to find the best combination of cost and performance for our products.

Several questions have been raised during the past ten years about NTA's safety. Without exception, we believe that each of the concerns that have been raised about NTA has been addressed. Its biodegradability, potential to carry heavy

metals, produce birth defects or human cancer -- each of these concerns has been refuted by long-term usage or testing. This position is shared by the scientists who have reviewed this matter for the governments of Canada, The Netherlands, Sweden and Finland which have approved the use of NYA in detergents, as well as by the Science Advisory Board of the International Joint Commission for the Great Lakes.

As a practical matter, NYA will only be able to be used in U.S. detergents if consumers are convinced of its safety. We hope that ultimately the true picture of NYA's safety can be conveyed to the U.S. public so that the advantages this ingredient has to offer can be realized in U.S. laundry detergents. We hope that this subcommittee hearing will contribute to that objective.

EDITOR'S NOTE: The following is a list of materials which Procter & Gamble submitted to the Subcommittee as supporting documents, but which are not reprinted here because of their voluminous nature. Copies may be reviewed at the subcommittee's offices.

THE PROCTER AND GAMBLE COMPANY TESTIMONYSUPPORTING DOCUMENTS

Submitted To
 Subcommittee on Oversight and Investigation
 Of The
 Committee on Interstate and Foreign Commerce
 June 26, 1980

1. Thayer, F. S. and C. J. Kamler, "Current Status of the Environmental and Human Safety Aspects of Nitrilotriacetic Acid (NTA)," *Critical Reviews in Environmental Control*, 3(4), Sept. 1973, pp. 375-604.
2. Nison, G. A., Z. V. Buchler and R. J. Nisvenhuis, "Two-Year Rat Feeding Study with Trisodium Nitrilotriacetate and Its Calcium Chelate," *Toxicology & Applied Pharmacology*, 21, 1972, pp. 244-252.
3. Lijinsky, W., M. Greenblatt and C. Kominoni, "Brief Communication: Feeding Studies of Nitrilotriacetic Acid and Derivatives in Rats," *Journal of the National Cancer Institute*, 50 (4), April 1973, pp. 1061-63.
4. Greenblatt, M. and W. Lijinsky, "Carcinogenesis and Chronic Toxicity of Nitrilotriacetic Acid in Swiss Mice," *Journal of the National Cancer Institute*, 52 (4), April 1974, pp. 1323-26.
5. NCI, "Bioassays of Nitrilotriacetic Acid (NTA) and Nitrilotriacetic Acid, Trisodium Salt, Monohydrate for Possible Carcinogenicity," *National Cancer Institute Carcinogenesis Technical Report Series No. 6*, January 1977.
6. IJC Report to the Great Lakes Research Advisory Board of the International Joint Commission on the Health Implications of NTA, May 1977.
7. Anderson, R. L. and R. L. Kamerva, "Effect of Nitrilotriacetate (NTA) on Cation Balance in the Rat," *Food Cosmet. Toxicology*, 16, 1978, pp. 563-68.
8. Anderson, R. L. and R. L. Kamerva, "Hypercalcaemia and Crystalluria During Ingestion of Dietary Nitrilotriacetate," *Food Cosmet. Toxicology*, 16, 1978, pp. 569-74.
9. Anderson, R. L. and R. L. Kamerva, "Comparisons of Response of Fischer-344 & Charles River Rats to 1.5% Nitrilotriacetic Acid and 2% Trisodium Nitrilotriacetate, Monohydrate," *Food Cosmet. Toxicology*, 17, 1979, pp. 137-40.
10. Anderson, R. L. "The Relationship of Insoluble Nitrilotriacetate (NTA) in the Urine of Female Rats to the Dietary Level of NTA," *Food Cosmet. Toxicol.*, 18, 1980, pp. 59-64.
11. Anderson, R. L. "A Comparison of the Effects of Nitrilotriacetate on Cation Disposition and Urinary Tract Toxicity," submitted for publication to: *Food Cosmet. Toxicol.*, June 16, 1980.

12. Report from the Consultative Group for the Reduction of Phosphate, (Netherlands) Jan. 1980.
13. Malaiyandi, M., D. T. Williams and R. O'Grady, "A National Survey of Nitritotriacetic Acid in Canadian Drinking Water," *Environmental Science Technology*, 13 (1), Jan. 1979, pp. 59-62.
14. Woodiwiss, C. R., R. D. Walker and F. A. Brownridge, "Concentrations of Nitritotriacetate and Certain Metals in Canadian Wastewaters and Streams: 1971-1975" *Water Research*, 13, 1979, pp. 599-612.
15. Matheson, D. W., "Nitritotriacetate (NTA) in the Canadian Environment," *Inland Waters Direct., Water Qual. Br. Environment Canada, Sci. Ser. No. 74*, 1977.
16. Anderson, R. L., "Discontinuities in Dose/Response Curves for Toxicological Tests," *Soap/Cosmetics/Chemical Specialties*, pp. 36-41, April 1979.
17. Scharpf, L. G., Jr., "Is NTA a Genetic Risk?" Presented at the Environmental Mutagen Society Meeting, Atlanta, Georgia, March 14, 1976.
18. Scharpf, L. G., Jr., "Health Effects of NTA," Presentation to IJC, Oct. 13, 1976.
19. Procter & Gamble Statement, "NTA and Carcinogenesis--The Dose Response Curve," March 13, 1979. (Submitted to NCI)
20. Anderson, R. L., "Relationships Between NTA Induced Alterations in Mineral Metabolism and Urinary Tract Toxicity Including Neoplasms in the Rat," July 24, 1979. (Submitted to NTP)
21. Review of P&G Statement Regarding Carcinogenicity of NTA, R. A. Goyer et al, *National Toxicology Program*, Jan. 24, 1980.
22. EPA Risk Assessment, "Final Report: NTA, April 22, 1980." (P&G Comments Appended)
23. Environmental Monitoring of Current NTA Concentrations in U.S. Waters.
24. NTA Bibliography from "Mucicola, Horacio A., "Nitritotriacetic Acid as a Chelating Agent: Applications, Toxicology and Bio-Environmental Impact," *Toxicological and Environmental Chemistry Reviews* 2, 99-161 (1974).
25. Report to the Great Lakes Research Advisory Board of the International Joint Commission on the Ecological Effects of Non-Phosphate Detergent Builders: Final Report on NTA, 1978.
26. Environmental Safety of NTA: Procter and Gamble Summary, June 13, 1980.
27. Procter & Gamble Statement, "Projected Levels of NTA in U.S. Waters Based on 1979 Market Volume Data."
28. Procter & Gamble's Perspective Regarding the Nine Recommendations for Additional Research on NTA by the International Joint Commission Task Force on the Ecological Effects of Non-Phosphate Detergent Builders.
29. Comment, *Water Research* 14 (1) 95-101 (1980).

THE PROCTER & GAMBLE COMPANY

IVORYDALE TECHNICAL CENTER

CINCINNATI, OHIO 45217

May 27, 1980

Dr. Warren Muir
Deputy Assistant Administrator for
Testing and Evaluation
U. S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

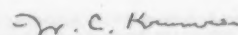
Dear Dr. Muir:

This is to request clarification of one part of the letter addressed to me by Mr. Steven D. Jellinek dated May 27, 1980 on the subject of the use of nitrilotriacetic acid (NTA) in laundry detergents. As the accompanying Fact Sheet pointed out, Procter & Gamble and Monsanto sought Federal guidance on the current advisability of lifting the voluntary abstention on the use of NTA in detergents in the U. S.

Since we had only asked for review of NTA for use in conventional laundry detergents, it is our understanding that you have not reviewed the use of NTA in other products. Therefore, we are surprised by the second recommendation in Mr. Jellinek's letter which is "NTA should not be used in shampoos, foods, hand dishwashing detergents, and other consumer products designed to have direct dermal or oral exposures." In EPA's Draft Final Report: NTA, dated April 22, 1980 which was released last week, your risk assessment for the use of NTA in conventional laundry detergents included consumer exposure to the expected low levels in drinking water, as well as the normal uses of a conventional laundry detergent; machine laundry, hand laundry and occasional hand dishwashing.

As the result of our telephone conversation today, it is our interpretation of this recommendation that since you have not reviewed NTA for use in products other than in conventional laundry detergents, you would prefer that anyone formulating products specifically designed for these other purposes review with you the data supporting these uses before marketing of such products. If this is indeed the proper interpretation, we would appreciate it if you would confirm this in a letter to me.

Sincerely,



W. C. Krumrei, Senior Director
Research & Development Department

WCK:mat

cc: Mr. Steven D. Jellinek, Assistant Administrator
for Pesticides and Toxic Substances

best copy available

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

May 30, 1980

Mr. William C. Krumrei
Procter and Gamble Company
Ivorydale Technical Center
5299 Spring Grove Avenue
Cincinnati, Ohio 45217

Dear Mr. Krumrei:

This is to confirm my comments in our telephone conversation of May 27, 1980, and to respond to your letter of the same date.

You have raised a question concerning the interpretation of the second recommendation in Mr. Jellinek's letter to you of May 27, 1980, on the subject of the use of NTA in laundry detergents. This recommendation reads, "NTA should not be used in shampoos, foods, hand dishwashing detergents, and other consumer products designed to have direct dermal or oral exposures."

We have not conducted thorough risk assessment for products other than conventional laundry detergents with their customary uses of machine laundry, hand laundry, and occasional hand dishwashing. Because of the chemical properties of NTA it was projected that it might have applications in a wider range of consumer products. Given the toxicological properties of NTA and the limited scope of our risk assessment, we felt it prudent to recommend that NTA not be marketed in other products specifically designed for food use, shampoos, or other prolonged and frequent dermal or oral exposure without our having an opportunity to conduct a full assessment of any data supporting such uses before marketing.

I hope this clarifies your question on this subject.

Sincerely,



Warren R. Muir
Deputy Assistant Administrator
for Testing and Evaluation

Mr. MAGUIRE. Thank you.
Mr. Throdahl?

TESTIMONY OF MONTE C. THRODAHL

Mr. THRODAHL. Thank you. I, too, am pleased to be here today to testify before you and the scientists and experts from elsewhere. I am submitting separately a written statement. I will now try to summarize this subject as quickly as I can.

Mr. MAGUIRE. Your prepared statement in its entirety will be made part of the record [see p. 99].

Mr. THRODAHL. The most important message that I would like to leave with you is this: Used in detergents, we believe that NTA poses no threat to people or the environment. It is readily biodegradable. It can only be found in the environment in trace amounts—in parts per billion. I would like to tell you why we believe this to be true.

Whenever we at Monsanto or any responsible chemical company decide to develop a product, a large part of the research is devoted to understanding the potential long-term effects of that product. Almost by definition, health and environmental data for new products must be obtained from laboratory experiments. Occasionally we do have some real world experience with a substance upon which we can base our own assessments. Such a situation exists with NTA. Not only do we have extensive laboratory data, but we have 8 years of statistics collected from Canadian washday experiences as well.

This morning I would like to describe some of the laboratory testing and the assessments that NTA has undergone in order to be judged environmentally safe. I will also describe the way real-life data were collected in Canada since 1972. Finally, I will review the chain of events that led up to the recent EPA decision and explain why Monsanto believes that this product should be reintroduced in the U.S. marketplace.

Scientists assessing the environmental acceptability of a product like NTA generally want answers to two questions:

First, what concentrations of the material will be found in the environment?

Second, what concentrations of the material cause effects on important organisms?

Monsanto began producing NTA in the late 1960's. Since then the extensive additional studies on NTA have made it something of a model, we believe, for environmental research.

Scientists at Monsanto, Procter & Gamble, the U.S. Environmental Protection Agency, the Canadian Government, and at several universities have conducted a full complement of environmental fate and environmental effects tests on NTA. Let me list some of them for you, notwithstanding what may have been said earlier.

Biodegradation tests took place in sewage treatment plant effluent, natural river waters, septic tanks under anaerobic conditions, and in ocean water or salt water.

Second, other experiments were concerned with the degradation of NTA in sunlight, by ozone, by chlorine, and in soil.

Third, microbes which consume NTA in the environment were identified and determinations were made as to how fast it degrades under different circumstances.

Fourth, still other experiments involved what complexes NTA forms with metal ions in the environment and how these influence the rate of disappearance.

Fifth, toxicology studies considered the effects of NTA on virtually every aquatic organism ever used for a test species. These organisms range from fly larvae to rainbow trout.

Those are the laboratory experiments. The Canadian environmental scientists added to these data with 8 years of observing NTA in the environment. They have measured NTA in sewage and in rivers that have received treated waste water. They have also analyzed water samples from ponds, lakes, and wells. From these studies there are some other conclusions that we can draw.

First, NTA readily breaks down in the environment to nitrogen, carbon dioxide, and water.

Second, NTA is practically nontoxic to fish and invertebrates. It neither retards the growth of desirable algae nor promotes undesirable species.

Third, Canadian data show that in fact NTA is readily degradable in salt water, cold water, and under anaerobic conditions, a conclusion which refutes some of the laboratory data.

Canadian studies also showed that NTA exists in Canadian drinking water, but in amounts so small as to be insignificant. The 2.8 parts per billion concentration exists in drinking water only because NTA is constantly being released into the environment. Moreover, this minute concentration is really below the levels which most sophisticated analytical equipment could identify just a few years ago.

Canadian Government publications suggest that the levels of NTA in the environment have tended to decrease over the years, even though the use has increased in the same time.

There are two overall conclusions we can draw from all of this. The first is that NTA presents no threat to the environment. Second, EPA officials had ideal circumstances in which to make their decision. That is, experimental data alone often leaves questions, but experience added to the experiment has provided a sound base for estimating long-term health and environmental effects.

Continuing, some 5 years ago the Great Lakes Research Advisory Board of the International Joint Commission set up two task forces to review human health and environmental implications of NTA in detergents.

The reports of these task forces were both positive toward NTA and led to a recommendation by the Joint Commission in mid-1978 that NTA be considered for use in the United States. Monsanto visited EPA at that time and requested that the agency issue an opinion on NTA's use in detergents as the IJC recommended.

EPA scientists carried out a thorough risk assessment with the data generated from the task forces as well as from information supplied by ourselves, by Procter & Gamble, and by others. Their conclusion, with which you now all are familiar, was not to oppose the reintroduction of NTA as an ingredient in U.S. detergents.

It has been said before, but I will repeat once more, that EPA is not the only Government agency which has been evaluating NTA. Finland, Sweden, Norway, all have approved NTA and earlier this year the Government of the Netherlands concluded an extensive review of alternates to phosphates in detergents and decided to allow the use of NTA in Dutch detergents.

Even though the environmental research on NTA was conducted outside the jurisdiction of any specific U.S. law or regulation, it obviously has been proven safe enough to meet the requirements of at least five other nations, as well as to receive tacit approval from the EPA.

NTA was a component of U.S. laundry detergents before the Toxic Substances Control Act became law. Its reintroduction now would take place before any significant new use rules are promulgated pursuant to section 5(a)(1)(B) of the act. However, were those rules in effect today and made specifically applicable to the use of NTA in detergents, we believe that neither the assessment nor the conclusions which EPA reached would have been fundamentally different.

As I suggested at the outset of my testimony, laboratory experiments can only simulate experience. With NTA we have a situation where data from the real world are available, are relevant, and do confirm laboratory predictions. This type of information should be and has been the basis for EPA's risk assessment. It shows that NTA, a very effective laundry detergent ingredient, presents an extremely low, if any, risk for consumer use.

Since the introduction of NTA, the Health Protection Branch of the Canadian Government has made a constant assessment and reassessment of the significance of NTA in the environment. We think this is as it should be.

Environmental testing should continue well past introduction of a material in the marketplace. Upon reintroduction of NTA into the United States, Monsanto is prepared to continue to monitor the waterways, sewage treatment plants, and the aquatic plant and animal life. We think in this way we can provide the U.S. Government and the American people with assurance that they and their environmental surroundings are protected.

In closing, Mr. Chairman, may I say that we at Monsanto will stand ready to help you and your subcommittee in any way possible in evaluation of the information that has been provided.

Thank you.

[Testimony resumes on p. 105].

[Mr. Throdahl's prepared statement and attachments follow:]

REVIEW OF EPA ACTION CONCERNING NTA IN LAUNDRY DETERGENTS

TESTIMONY OF MONTE C. THRODAHL, SENIOR VICE PRESIDENT,
MONSANTO COMPANY

My name is Monte C. Throdahl. I am Senior Vice President of Monsanto Company with responsibility for the Environmental Policy Staff.

I am pleased to be here today to testify before the distinguished members of this Subcommittee, as well as scientists and experts from the Environmental Protection Agency. The subject of the use of NTA in detergents is a matter of considerable importance. I am glad to have this opportunity to address myself to that subject.

The single most important message I would like to leave with you this morning is this: Used in detergents NTA poses no threat to people or the environment. It is readily biodegradable; that is, only trace amounts can be found in the environment.

Now, I would like to tell you how we know that is true.

Whenever Monsanto -- or any responsible chemical company -- decides to develop a product, a large part of the research is devoted to understanding the potential long-term effects of that product. Almost by definition health and environmental data for new products must be obtained from laboratory experiments. Occasionally, however, a situation occurs where we do have real world experience with a substance upon which we can base our assessments.

Such a situation exists with NTA. Not only do we have extensive laboratory data; we have eight years of statistics collected from Canadian washday experience as well.

This morning I will describe some of the laboratory testing and assessment that NTA has undergone in order to be judged environmentally safe, as well as the way real life data was collected in Canada since 1972. I will review the chain of events that led up to the recent EPA decision and explain why Monsanto believes the product should be reintroduced into the U.S. marketplace.

EPA's decision not to regulate use of NTA in detergents was based on a great many studies and a great deal of information. Most important is the fact that since the U.S. detergent industry ceased using NTA a decade ago, it has become a major ingredient of Canadian laundry detergents and has been used in millions of Canadian households. As a result Canadian scientists have been able to supplement the extensive laboratory work with data compiled from actual experience.

Scientists assessing the environmental acceptability of a product like NTA generally want to answer two questions:

1. What concentrations of the material will be found in the environment?
2. What concentrations of the material cause effects on important organisms?

Other kinds of information are developed to assess effects on humans. You have heard in other testimony about the tremendous amount of this data that exists to assess any hazard associated with NTA's use in laundry detergents.

Monsanto began producing NTA in the late 1960's at the request of customers who wanted an alternative to phosphates in laundry detergents. At that time, the idea of environmental safety testing was very new. By today's standards only basic environmental tests had been completed when NTA was introduced to the supermarket shelves. Since then, however, the extensive additional work on NTA's environmental characteristics has made it something of a model for Monsanto environmental research.

Scientists from Monsanto, Procter & Gamble, the U.S. Environmental Protection Agency, the Canadian government, and at several universities have conducted a full complement of environmental fate and effects tests on NTA.

Biodegradation tests took place in sewage treatment plants, natural river waters, septic tanks (anaerobic conditions) and ocean (salt) water. Other experiments were concerned

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with degradation of NTA in sunlight, by ozone, by chlorine and in soil. Microbes which consume NTA in the environment were identified and determinations were made as to how fast it degrades under different circumstances. Still other experiments involved what complexes NTA forms with metal ions in the environment, and how these influence the rate of disappearance.

These tests showed that NTA readily breaks down in the environment to nitrogen, carbon dioxide and water. A scheme depicting the common means of breakdown appears in Exhibit 1.

In other experiments, aquatic toxicologists looked at the effects of NTA on virtually every aquatic organism ever used for a test species. These organisms range from fly larvae to rainbow trout. (See Appendix A).

The results of this work showed that NTA is practically non-toxic to fish and invertebrates. It neither retards the growth of desirable algae nor promotes undesirable species.

In addition to the laboratory studies, Canadian environmental scientists have measured NTA in sewage and in rivers that receive treated waste water (effluent). They have analyzed water samples from ponds and lakes and wells. Their data showed that in fact NTA is readily degradable in salt water, cold water, and under anaerobic conditions (see Appendix A).

Canadian studies also showed that NTA exists in Canadian drinking water -- but in amounts so small as to be insignificant. The 2.8 parts per billion concentration of NTA in drinking water exists only because NTA is constantly being released into the environment, and would disappear if NTA were withdrawn. Moreover, this concentration is below levels which the most sophisticated analytical equipment could identify only a few years ago.

Canadian government publications suggest that levels of NTA in the environment have tended to decrease over the years, even though use has increased in the same time.

The conclusion we can draw from all of this is that NTA presents no threat whatsoever to the environment. It also suggests that EPA officials had ideal circumstances in which to make their decision. Experimental data alone often leaves questions. Experience added to experiment has provided a sound base for estimating long-term health and environmental effects.

Issues related to the environmental acceptability of NTA have received exhaustive study over the past fifteen years. The information thus obtained has been assessed in depth in at least three published documents: EPA's recent Risk Assessment; the International Joint Commission's "Ecological Effects of Non-Phosphate Detergents Builders: Final Report on NTA"; (Appendix A) and Environment Canada's "NTA - An Ecological Appraisal." (Appendix B). Together these present as comprehensive an evaluation of environmental safety as one can hope to achieve; they include the results of Monsanto's safety studies, as well as those of others.

In addition, two reports on the levels of NTA in Canadian waters have appeared and are attached as Appendices "C" and "D". The work described in these two reports is based on analytical technology developed by Monsanto. Further information on this subject can be found in the International Joint Commission Report referred to above.

Five years ago, the Great Lakes Research Advisory Board of the International Joint Commission set up two task forces to review human health and environmental implications of NTA in detergents.

The reports of these task forces were both positive towards NTA, and led to a recommendation by the Joint Commission in mid-1978 that NTA be considered for use in the U.S. Monsanto visited EPA at that time and requested that the Agency issue an opinion on NTA's use in detergents as IJC recommended.

EPA scientists carried out a thorough risk assessment with the data generated from the task forces as well as other data supplied by Monsanto, by Procter & Gamble, and others. Their conclusion, which was issued a few weeks ago, was not to oppose the reintroduction of NTA as an ingredient in U.S. detergents.

Incidentally, EPA isn't the only government agency which has been evaluating NTA. Early this year, the government of the Netherlands concluded an extensive review of alternatives to phosphates in detergents, and decided to allow NTA's use in that country.

Even though the environmental research concerning NTA was conducted outside the jurisdiction of any specific U.S. legislation or regulation, it obviously has met the requirements of several other nations, as well as to receive tacit approval from EPA.

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NTA was a component of U.S. laundry detergents before the Toxic Substances Control Act became law. Its reintroduction now would take place before Section 5a1B, the Significant New Use Rules, are promulgated. However, were those rules in effect and made specifically applicable to use of NTA in detergents, we believe that neither the assessment nor the conclusions which EPA reached would have been fundamentally different.

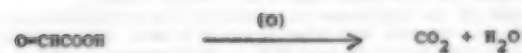
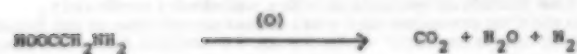
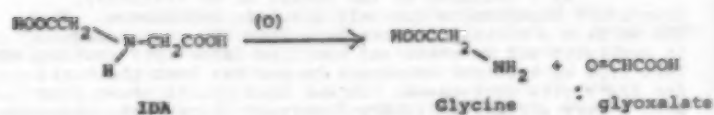
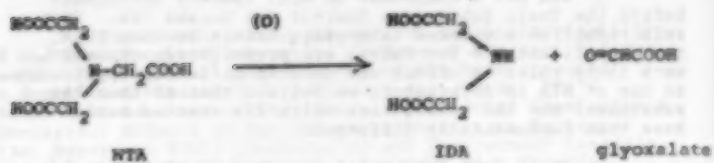
Ample data were available upon which EPA could base its assessment of NTA. More importantly, extensive laboratory data was supplemented by actual use experience.

As I declared at the outset of my testimony, laboratory experiments can only simulate experience. With NTA we have a situation where data from the real world is available and relevant and confirms laboratory predictions. This type of information should be and has been the basis for EPA's risk assessment. In our opinion, it shows that NTA, a very effective laundry detergent ingredient, presents negligible risk for consumer use.

Since the introduction of NTA, the Health Protection Branch of the Canadian government has watched it closely, making constant assessment and reassessment of the significance of NTA in the environment. This is as it should be. Monsanto also believes that environmental testing should continue well past introduction of a material into the marketplace. Upon reintroduction of NTA into the U.S. environment, Monsanto is prepared to continue to monitor the waterways, the sewage treatment plants and the aquatic plant and animal life. This way we can provide the U.S. government -- and the American people -- with assurance that they and their environmental surroundings are not being harmed.

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EXHIBIT 1



LIST OF APPENDICES A THROUGH D

APPENDIX A--"Ecological Effects of Non-phosphate Detergent Builders: Final Report on NTA," from the Task Force on Ecological Effects of Non-phosphate Detergent Builders, to the Great Lakes Research Advisory Board of the International Joint Commission--December 1978

APPENDIX B--"NTA (Nitrilotriacetic Acid)--An Ecological Appraisal" Economic and Technical Review Report, EPS 3-WF-76-8, Water Pollution Control Directorate--November 1976, Canadian Environmental Protection Service

APPENDIX C--"Nitrilotriacetic Acid (NTA) in the Canadian Environment," Scientific Series No. 74, Inland Waters Directorate, Water Quality Branch, Canadian Department of Fisheries and the Environment--1977

APPENDIX D--"A National Survey of Nitrilotriacetic Acid in Canadian Drinking Water," an article from Vol. 13, No. 1, January 1979, American Chemical Society

Mr. MAGUIRE. Thank you, Mr. Throdahl.

In view of the fact that time is moving along, the Chair is going to ask members to limit themselves to 5 minutes each round.

Mr. LENT?

Mr. LENT. Thank you, Mr. Chairman.

Mr. Krumrei, I am intrigued by those bottles. I wonder if you will straighten me out.

As I understand it, both bottles contain NTA. The big bottle is to represent the level at which humans would have to consume that bottle every day for 75 years in order to what?

Mr. KRUMREI. In order to reach the level that was fed to rats to get the effect level.

Mr. LENT. Fed to rats under the NCI study of 1977?

Mr. KRUMREI. Yes, sir.

Mr. LENT. That obviously is a greater level than was actually fed to the rodents.

Mr. KRUMREI. Oh, yes.

Mr. LENT. You are making an extrapolation of the human being as compared to the rodent.

Mr. KRUMREI. Yes, sir, because of the difference in weight. This is the amount that would need to be used or ingested by a human every day for 75 years of his life to equal the amount that the rats were fed.

This smaller bottle contains the amount that the human will actually be exposed to for an entire 75 years of drinking water with NTA at the Canadian level.

Mr. LENT. With respect to the smaller bottle, can you tell us how many milligrams or how much is in that for the record? The record cannot indicate how big the bottles are.

Mr. KRUMREI. Could you please answer that?

Mr. WINTERS. I am Dr. Winters.

The exact weight is 0.15 grams. That would be the quantity accumulated over all the times that you drank these 2 liters every day for a lifetime.

Mr. KRUMREI. A 75-year lifetime.

The other one contains 51.8 grams.

Mr. LENT. The larger bottle?

Mr. KRUMREI. The larger bottle, yes, sir.

Mr. LENT. How can you be sure that 0.15 grams is the amount of NTA that a human being will consume in a lifetime?

Mr. KRUMREI. This is based on the level of NTA in Canadian waters, the average level of 2.8 parts per billion, with the assumption that the normal human drinks 2 liters of water per day for 75 years. EPA's risk assessment was based on a 75-year life.

Mr. LENT. Wouldn't it make a difference where you live as to how many grams would be in that bottle?

Mr. KRUMREI. Oh, yes, sir. The maximum that was ever found in drinking water in Canada was approximately 10 times this level.

I believe the numbers are correct, and my colleagues will make sure of this. Forty percent of the drinking water samples that the Canadian Government tested contained no NTA at the level of sensitivity of the method, which was 0.2 parts per billion.

Mr. LENT. I think you leave us somewhat confused, at least this member, as to how a number of competent scientists review the same information and come to differing conclusions regarding NTA as a cause of cancer. You say that NTA cannot cause cancer through its use in detergents while others call it a weak carcinogen and give an estimate that one in so many million people will develop cancer through its use in detergents.

Could you perhaps enlighten us and try to explain the apparent inconsistency?

Mr. KRUMREI. No. 1, I think it would be very difficult to get any group of scientists to agree on any single issue. You are dealing with interpretation of facts.

For this purpose, however, we considered all of the information available. Using the best acceptable theory of carcinogenesis, which is that if it is not a mutagen it is not likely to be a carcinogen, and inasmuch as we and the Government and others have run 25 mutagenic studies with 17 different test systems, we are fairly confident this is not a mutagen. In order to act as a carcinogen, it had to have had that as a precursor.

This information was discussed with the Dutch Government. They were aware of it. They came to the same conclusion that we did.

Mr. MAGUIRE. The gentleman's time has expired.

The gentleman from Connecticut is recognized.

Mr. MOFFETT. Thank you, Mr. Chairman.

Gentlemen, you were here this morning, I noticed, for the testimony of our earlier witnesses. Let me first ask Dr. Krumrei a question.

In your testimony you emphasize this, and I quote: "The scientific data base supporting our conclusions on the safety of NTA is exhaustive and we take particular pride in the fact that this data base has been subjected to peer review not only within our compa-

ay, but by other scientists and governmental experts in the United States and several other countries."

How can you reconcile that statement and the testimony which we received earlier today from Dr. Perry with your statement that NTA "exhibits no buildup in surface or groundwaters" and "does not adversely affect sewage treatment"?

Mr. KRUMREI. I do not know the data to which Dr. Perry has been exposed. However, the data base that we have I believe is considerably larger. That is the entire data base that I believe Mr. [unclear] quoted in part from the EPA risk assessment document.

I would also like to ask Dr. Golberg, who is probably one of the outstanding toxicologists in the country, to comment on how we can come to different points of view, if I may.

Mr. MOFFETT. Please.

Doctor, welcome.

Dr. GOLBERG. Thank you, Mr. Chairman.

If I may, I would like to mention that I was an expert consultant of the task force of the Great Lakes Commission on NTA, so I am fairly familiar with the scientific data. I am going to comment only on the health effect aspect.

Mr. MAGUIRE. Excuse me. Ordinarily you are located where?

Dr. GOLBERG. I am president of the Chemical Industry Institute of Toxicology in Research Triangle Park, N.C.

Mr. MAGUIRE. Do you have any relationship with P&G specifically?

Dr. GOLBERG. Not at all.

Mr. MAGUIRE. But you do to the industry group to which you just alluded?

Dr. GOLBERG. Yes. We are an independent, nonprofit organization but we are supported by 35 chemical companies.

Mr. KRUMREI. We are not a member of that industry group, sir.

Mr. MAGUIRE. Thank you very much.

Dr. GOLBERG. I would take as my point of departure the evidence for lack of mutagenic activity which has been referred to and Dr. Rall's comment that this form of cancer produced by NTA, and I am quoting him now, "is a slightly different kind of cancer." The fact of the matter is that if one looks at it from the point of view of experience, with the kind of phenomena elicited by NTA, one realizes that one is dealing with a situation where there are primary and secondary pathological effects.

Just as an example for the layman, I would point out that in the days before modern burn therapy was instituted it was common to have severe scars at the sites of burns. It was not at all uncommon to have cancer developing in those scars. That illustrates the fact that unless you have the primary event, namely, the scar, you do not get the secondary event; namely, the cancer developing in it. This is essentially what we are dealing with here.

Mr. MAGUIRE. You do not get it or you may not get it?

Dr. GOLBERG. Cancers, of course, occur spontaneously, but the coincidence of the cancer in the burn scar was obviously something of great significance.

Mr. MAGUIRE. All I am suggesting, if I may, is that you may get cancer where there is such an event or you may not. You may get it or not without such a scar.

Dr. GOLBERG. That is so. In the particular case with which we are concerned, we have a situation where these huge excesses of NTA administered to the animals elicited very severe kidney damage and elicited a variety of other phenomena which I regard as being the primary events. Without these, I do not consider that the secondary events, namely, kidney cancer or bladder cancer, could have been produced.

Mr. MOFFETT. Then this is a hypothesis, Doctor?

Dr. GOLBERG. I have had considerable experience with similar situations, not this particular one.

Mr. MOFFETT. That is useful.

You heard me earlier perhaps say that I am very concerned about the NTA impact on groundwater. This question that I have asked is asked in that vein.

You, Doctor, have just mentioned the Great Lakes research. It is attached to the testimony of Mr. Throdahl.

On page 74 of that document—and I am sure you are very familiar with it—it says, and I quote:

"In summary, NTA levels in groundwater may be substantial, particularly in cases where contamination by domestic sewage is evident. Small, privately constructed wells are more likely to be contaminated than municipal groundwater sources."

That troubles me. If you can put my concerns to rest, I would be thrilled. It does trouble me. Here is a study that is being cited by many of you witnesses and it seems to indicate that we have a problem. Am I reading it incorrectly?

Dr. GOLBERG. With respect, Mr. Moffett, I am not an authority on environmental factors.

Mr. MOFFETT. I am not asking you necessarily, Doctor. I am asking anyone at the witness table.

Mr. THRODAHL. May I respond?

Mr. MOFFETT. Please.

Mr. THRODAHL. My associate, Dr. James Wilson, who is with me, is manager of research and development, product acceptability and environmental affairs for Monsanto.

He tells me that NTA is known—it is factual—to decompose in properly operating septic tank field systems, but in wells that tap an overloaded septic system, the bacteria from the sewage will be a very serious situation and far outweigh the alternative, as you might suspect, if indeed there is some residual NTA. He suggests that the bacterial question would be far greater, if that is helpful.

Mr. MOFFETT. That is somewhat helpful.

We are sitting here as laymen, and you all know that. We have a panel of scientists who come before us and say perhaps EPA did not do its homework in a thorough enough fashion. Then this panel comes along and says, "Well, really, everything is OK."

It is rather difficult because we do have the public trust to try to uphold here. We are not trying to give the industry a hard time for the sake of it.

I look at these figures of 60 million pounds of NTA, as I understand maybe 10 of which stays in the United States right now, and there is a possibility of that mushrooming to 150 million—if you look at the top level of that, it could be 1 billion pounds, if I am not mistaken.

I say to myself, "Well here is an industry that sat on December 17, 1971, with the Surgeon General."

Mr. KRUMREI. 1970.

Mr. MOFFETT. 1970, excuse me. They sat with the Surgeon General. In that period of time we had the Council on Environmental Quality involved, the National Cancer Institute, the Surgeon General, Dr. Rall's agency, the EPA. Why not go back to them?

This subcommittee could require that these agencies get together and evaluate this. Why in the world don't you inquire further about something that does provoke this kind of controversy. I am not saying you are wrong, but if we are so convinced let's go back and touch base with those same agencies. What is wrong with that? That is the plea that I would make—that we not go back on the market without having some of these other people check off on this.

Your reaction might be, "Here we go again with another Government review that takes forever." We can ride herd on them to assure that it is done in fairly rapid order.

I would hope, Mr. Chairman, that we could get the industry people, particularly, to agree to at least that much today, unless you totally discount the testimony that we have had earlier. Maybe they can speak to that.

Mr. MAGUIRE. I think it is a good suggestion. I note they have included in their testimony statements to the effect that they are not now using NTA and they have not made a determination, if I read the statements correctly, that they will in fact use it. Therefore, perhaps we could ask on behalf of us here, given the testimony that has been heard today, whether there are in fact any unsettling aspects of this that occur to those who are at the table now and, if so, whether they would be responsive to the gentleman from Connecticut's suggestion.

Mr. LENT. I would like to be heard on this for a moment. I have a question.

As I understand it, wasn't EPA's action here in issuing this risk assessment perfectly appropriate and what we had in mind and in accordance with the TSCA legislation?

Mr. MOFFETT. That is not what this gentleman had in mind.

Mr. LENT. In other words, we have done all this once. Now the purpose of this oversight meeting is to determine whether EPA came to their conclusion in some sort of a disorganized way or failed to follow normal regulatory procedures.

To say let's go back and put these gentleman on the spot and say, "Will you agree to go back and let's have another 5-year study," I think that is perhaps unfair to them at this particular time. They have been through this.

Mr. MAGUIRE. The gentleman is fully entitled to his interpretation of whether or not EPA acted in a proper fashion under the law. We are going to have the EPA representatives before the committee after this panel. We can fully explore those issues.

In my opening statement I suggested that it seemed to me that there were some serious issues relating to Federal cancer policy involved here not only with respect to the compound and the regulatory decisions on it, but also with respect to the process. One of the witnesses this morning in fact spent a great deal of time

developing a critique of EPA's behavior as against the provisions of the law. Clearly, these are issues that are before the committee and one of the reasons we are having this hearing today.

Mr. LENT. In the interest of orderly procedure, it would seem to me that we ought to wait to determine, after we have conducted our oversight and completed this investigation, whether there was anything amiss in EPA's handling of this particular risk assessment, rather than at this juncture, before we have made that determination, asking the question of the industry as to whether or not they would agree to go through another governmental regulatory procedure. We have not yet reached a conclusion that there was anything wrong with what the EPA did, have we or have we prejudged this to that extent?

Mr. MAGUIRE. The gentleman, of course, is fully entitled to his view that he does not wish to ask such a question at this point, but he is not the one who asked it. Mr. Moffett is the one who asked it. Witnesses will then have a choice as to whether or not to respond. I see at least three hands already at the table.

Mr. MOFFETT. Would you yield?

Mr. MAGUIRE. I yield to the gentleman.

Mr. MOFFETT. The gentleman from New York used the word "prejudged"—"prejudged this to that extent." It is not a matter of prejudging. The gentleman sat through the testimony this morning. Unless the gentleman is prepared to discount totally the testimony of the scientific panel—and he may well be prepared to do that, but I am not prepared to do that and I find myself confused.

Second, the gentleman mentions another regulatory proceeding. There was no regulatory proceeding that this industry went through. There was no APA-type of proceeding, a formal rulemaking, public hearings, or anything of that nature. The gentleman knows that.

I am not suggesting that right now at this instance that the industry say, "OK, we will do that," and the chairman bang the gavel and the hearing is over. I am just saying as a plea to the industry that they consider this; that's all.

Mr. MAGUIRE. I would like to reclaim my time and the prerogative of the Chair.

Mr. PEPPER. May I answer the question that was raised.

Mr. MAGUIRE. Yes, in just a moment if I can tie this up with my two colleagues here.

Obviously we will have plenty of time to discuss these and other matters during the course of the hearing and subsequently as the committee deliberates on the subject of the hearing. However, at this point it seems to be appropriate for members to ask questions. If the gentleman from Connecticut would like to restate his question or, absent that, if Mr. Pepper would like to respond, we would be happy to hear from either of them.

Mr. PEPPER. I would just like to make a comment on it.

First, I can readily understand why you would be confused if this is a fresh subject to you.

Mr. MOFFETT. Even if it were not a fresh subject, wouldn't I be confused? Couldn't I conceivably be confused?

Mr. PEPPER. Mr. Moffett, I do not feel confused on it, but, with all respect, I would imagine you have not been into this in a tremendous amount of depth. It is complex.

On your point, we would not have had any thought of reintroducing NTA in our detergents given the controversy that surrounded this subject and the request to withdraw it back in 1970, which we did not agree with but which we really had to do, without at least getting some advisory opinion from what we felt were the appropriate people in the Government. That, of course, is what has initiated our recontacts with the NCI and the EPA. What I want to convey to you is that we have been doing our best to get that overview on it through what we understand to be the appropriate channels.

Second, I really have not heard anything from the science panel today which, to the best of my knowledge, is something that has not before been before the groups of the Netherlands Government and the EPA in their analysis.

Mr. MAGUIRE. Mr. Pepper, did you or any employees of your company help the EPA write its analysis?

Mr. PEPPER. No. Mr. Krumrei are you talking about the risk assessment document, sir?

Mr. MAGUIRE. We have a letter dated April 27, 1979, from William D. Hopping of P&G to Justine Welch of EPA which contains a whole series of comments and recommended changes in the document that was under discussion at that time.

Mr. KRUMREI. In the original document?

Mr. MAGUIRE. Yes.

Mr. KRUMREI. As I understand it, the risk document was made public by EPA at a meeting of the Science Advisory Board on May 22, 1980. We ourselves then first saw a copy of this risk document on May 24, 1980.

Mr. MAGUIRE. As I understand it, there was a specific request from EPA to Mr. Hopping asking for his comments.

Mr. KRUMREI. EPA has made several requests to us over a period of several months for data because they knew we had quite a bit of data and had ready access to it and would save them some time and money getting it.

Mr. MAGUIRE. You did make suggestions on the draft which were incorporated, at least in part, by EPA; is that not true?

Mr. KRUMREI. We did not make comments to EPA on the risk assessment dated April 22, 1980. We did, however, make comments to EPA on April 27, 1979, on a draft report of an NTA human exposure document prepared by Midwest Research, Inc. for EPA. Since we had made the data available to EPA, we were specifically requested to aid in this effort. I do not know who else made comment.

Mr. MAGUIRE. We will explore this in greater detail.

Mr. MOFFETT. If we might, I want to understand what kind of process this was. Would some environmental group in the State of Connecticut have known about the EPA request for comments? Was it published somewhere?

Mr. KRUMREI. The EPA document?

Mr. MOFFETT. No, the requests for comments.

Mr. KRUMREI. I cannot answer that. I believe the document was made available to the public.

Mr. MOFFETT. It is a little unfair to ask you that.

Mr. KRUMREI. I cannot answer that. May I comment on one of the things you commented on about total usage? You indicated that it could possibly build up to a billion pounds. That was the number that was used earlier.

Back in 1970 when we were still using this material, we were at a very high phosphate level. We were anticipating that we would replace about half of the phosphates with NTA. Since then we have lowered our phosphate level dramatically, and we are not going to come anywhere near a billion pounds. I am talking about the total industry now.

Mr. MOFFETT. I was just trying to illustrate what to me was a rather large increase, even if you go to 150 million. This goes back to what you said. If in fact you are touching base with other agencies, are you going back to the Surgeon General? Has there been communication? Can you tell us about any letters or anything?

Mr. KRUMREI. We intend to go back to the Surgeon General.

Mr. MOFFETT. You do?

Mr. KRUMREI. Yes, sir.

Mr. MOFFETT. Before you make your final decision?

Mr. KRUMREI. We intend to go back to the Surgeon General to indicate to him all of our data. We have not yet done that because of all of the publicity.

Mr. MAGUIRE. I believe Dr. Lehne had his hand up a minute ago.

Dr. LEHNE. I just wanted to comment that the original panel concerned itself with the teratogenic problems. This carcinogenic situation is something entirely new. I do not believe the original panel would be qualified to reconvene and discuss this entirely new situation.

Mr. MOFFETT. I am not suggesting the same people.

Mr. KRUMREI. May I make one other suggestion, Mr. Chairman?

Mr. MAGUIRE. Yes.

Mr. KRUMREI. If you are going to order a relook at this, I urge that a science panel of outside, competent scientists be established, not just Government scientists but people who do not have an axe to grind, to look at what this means. I am talking about a science panel composed of the best people you can get together to help you make a judgment, if this is what you really want to do.

Mr. MAGUIRE. For myself, and I am sure I speak for the committee, I would think that is a very excellent suggestion.

Mr. LENT, in all fairness, inasmuch as we have exceeded our time over on this side of the aisle, I would like to call on you for another 5 minutes before I get to my own questions, if you would like.

Mr. LENT. Dr. Lehne, let me ask you a couple of questions. As I understand it, your firm, Church & Dwight, produces nonphosphate detergents, non-NTA detergents. Is that correct?

Dr. LEHNE. That is correct, sir.

Mr. LENT. You are a competitor of P&G?

Dr. LEHNE. Yes.

Mr. LENT. Your share of the market now is I think you said 1.3.

Dr. LEHNE. About 1.3, correct.

Mr. LENT. If NTA were to be approved for use in detergents, wouldn't that have a negative effect on the sales of Arm & Hammer detergent?

Dr. LEHNE. Not necessarily. We have not worked with NTA inasmuch as at the time we got into the detergent market it had already been voluntarily discontinued. We do not have any idea about its performance characteristics in our particular kind of detergent.

Mr. LENT. If NTA were to be approved for use in detergents, would it be probable that the Church & Dwight Co. would begin to produce it or would you stick with the bicarbonate soda?

Dr. LEHNE. I think we would certainly look at it, evaluate it, see what its benefits are and what kind of formulation within our cost parameters we could develop. We would compare that to the formulation we have now and any other new detergent builders or surfactants that would come on the market.

There is a constant evaluation of available materials. Reformulations and changes are constantly taking place. It may very well be that NTA could find a place if it were given a clean bill of health to be used by the industry.

Mr. LENT. I am just trying to determine what your role is on the panel. You are sort of not directly affected then by this controversy over NTA?

Dr. LEHNE. No, I am not. We are not. Some comments were requested concerning alternative builders. I just discussed some of the alternative builders, particularly the one that we use.

Mr. LENT. Have there been any studies, to your knowledge, performed on carbonates or bicarbonates to evaluate their possible carcinogenicity?

Dr. LEHNE. Yes. I believe this was all reviewed in the FDA GRAS review. Carbonates and bicarbonates are used as food additives. In order to clear them on the GRAS as food additives, teratogenicity, mutagenicity, and carcinogenicity have all been examined.

Mr. KRUMREI. Mr. Lent, would you yield for a question to the chairman?

Mr. LENT. That is up to the chairman.

Mr. KRUMREI. Mr. Chairman, may I ask a question? Dr. Golberg has a plane to catch. May he be excused from the panel?

Mr. MOFFETT [presiding]. Certainly. We thank you for your participation, Doctor, and for your patience today before the subcommittee.

Mr. KRUMREI. I am sorry, Mr. Lent. Thank you very much, Mr. Chairman.

Mr. LENT. Dr. Lehne, are the ingredients in your products equally effective in cleaning ability to NTA or to phosphates?

Dr. LEHNE. Cleaning ability is a difficult thing to evaluate. You have so many different conditions of operation, of clothes, of soils. There are conditions under which our material will perform as well or better than other detergents. There are conditions under which other detergents will perform better. We are satisfied that we have a product that does perform well for a large number of people, that it cleans effectively. It does have the disadvantage of redepositing some soils in extremely hard water, leaving a light film which may discolor colored fabrics.

Mr. LENT. Is it fair to say that the major suppliers of laundry detergents are not using the carbonates or bicarbonates as a builder?

Dr. LEHNE. In the nonphosphate areas they are using them because alternate builders have to be found. It is possible to develop and formulate a detergent, such as some of the liquid detergents, without builders. You have to compensate with other materials and a higher level of surface active materials. Competitive, major brands also use carbonates in the nonphosphate formulations.

Mr. LENT. If your cleaner is not as effective as phosphate or NTA in detergents, doesn't that encourage on the part of the housewife or househusband, whatever the case may be, the use by them of additional cleaning products in the laundry process that could add substantially to pollution?

Dr. LEHNE. It is possible and conceivable, of course. People's requirements of performance vary. Some people are happy with a lick and a promise. Others are extremely fussy, and they are going to use everything they can lay their hands on anyway.

The consumer finds the product that is satisfactory for his or her use with her laundry load, with her environment, with her daily needs. As a result, Arm & Hammer has found a small niche in the detergent area. It has its loyalties as well as the other major brands.

Mr. LENT. Mr. Throdahl, in your testimony you make constant reference to the Canadian data as justification for permitting NTA's expanded use in the United States. Yet, we heard from Dr. Karstadt at page 6 of her testimony reference to factors which might make the Canadian data of questionable validity in the United States.

Could you respond to those references, please?

Mr. THRODAHL. It is my understanding that the Canadian experience is located in urban areas which are quite comparable to what would be experienced in the United States on a population density basis. That is the basis for my justification.

Mr. LENT. Do you have protective measures that Monsanto employs for its own employees that handle this NTA?

Mr. THRODAHL. Yes, we do.

Mr. LENT. Will you describe them?

Mr. THRODAHL. The process itself, the actual chemical reaction, is entirely self-contained and sealed in the sense that there is no exposure to the individuals at that point. There are monitoring devices of many kinds, personal dosimeters and so on, which record levels of the reactants. That is no problem.

We are dealing with hydrogen cyanide, for example, in many other processes. We know how to handle that very safely.

The solid substance in the sodium salt is where the exposure is highest. Workers in that area wear protective clothing, protective masks, inhalation devices. They are required to shower thoroughly after working in that particular area. We also run medical monitoring checks as appropriate on such workers.

Mr. LENT. Has Monsanto been researching or testing possible alternatives to NTA? If so, would you discuss with us what these possible alternatives are and their drawbacks or advantages as compared with NTA?

Mr. THRODAHL. Yes, sir, we have. The number is legion, truly. When one gets to a point of selection from a huge number of possibilities, first of all, one must consider efficacy. Then one must consider the potential cost, even on an estimated basis. When one looks at efficacy and cost, raw material availability, environmental safety, and the like, NTA really stands head and shoulders above whatever would be second or third choices at this point in time.

We have carried some of those rather far in evaluations that would suggest that. These are not just paper studies.

Mr. LENT. I think it was on page 4 of your testimony that you said that the Canadian data show that NTA is readily degradable in salt water, cold water, and under anaerobic conditions.

Mr. THRODAHL. Yes, sir.

Mr. LENT. If we look at pages 4 and 5 of Dr. Karstadt's testimony, she refers to EPA findings which indicate questions about NTA degradation in saline water and under anaerobic conditions. Can you give us any explanation for that?

Mr. THRODAHL. I am not a specialist in that area. I would like to consult Dr. Wilson to see whether he can shed some light on it.

Mr. LENT. Dr. Wilson can respond directly.

Dr. WILSON. Basically this is a question of the difference between laboratory experiments and data extracted from use in the real world. In the laboratory we try as best we can to simulate the conditions which exist, but, as you know, we are not perfect. We cannot practically ever duplicate the variety of situations which will exist. We are not able to find all the different types of microbes which can possibly degrade a substance such as NTA, but they are there in nature.

The Canadians have found by actual measurement that NTA disappears from relatively anaerobic waters, from saline waters, and that it disappears regularly when the very cold winter conditions exist in the populated areas in southern Ontario. That is what we base the statement on.

Mr. LENT. Dr. Wilson, as long as I have you here, I have one final question in this time span.

What is your interpretation of the data on the carcinogenicity of NTA?

Dr. WILSON. Mr. Lent, that is something entirely outside my field of expertise. I cannot really comment.

Mr. LENT. I have no further questions at this time.

Mr. MAGUIRE. Mr. Throdahl, on page 3 of your testimony you state rather unequivocally, "NTA presents no threats whatsoever to the environment." You cite the International Joint Commission's Ecological Task Force in support of that conclusion. You include that report in appendix A.

Are you familiar with who the chairman of that task force was?

Mr. THRODAHL. No, sir.

Mr. MAGUIRE. It was Dr. Joseph Shapiro.

Mr. THRODAHL. I know the name, but I have not met him.

Mr. MAGUIRE. He is a distinguished scientist from the Limnological Research Center of the University of Minnesota.

I would like to ask unanimous consent that at this point in the record a letter from Dr. Shapiro to the subcommittee, dated June 23, 1980, be included in the hearing record.

[The letter referred to follows:]

As dictated
by Dr. Shapiro
over the telephone
June 23, 1980
to Debra Jacobson
of the Subcommittee
Staff.

June 23, 1980

Honorable Bob Eckhardt
Chairman
Subcommittee on Oversight
and Investigations
U.S. House of Representatives
Washington, D.C. 20515

Dear Mr. Eckhardt:

I have read Steven Jellinek's letter to Procter & Gamble Co. and have reviewed the report on NTA prepared by the EPA. I find that many of the same environmental concerns expressed in the IJC Task Force Report and discussed by me with Mr. Muir and Mr. Jellinek at a short meeting in 1979 are expressed once again in the EPA report but have not found their way into the letter to Procter & Gamble. This surprises me. As we stated in the IJC report, use of NTA does not appear to constitute an environmental hazard but because use in the United States would be on a much greater scale than hitherto we felt that its use here should be accompanied by specific studies to address the expressed concerns.

It is my opinion that the EPA letter to Procter & Gamble which does not require such studies but suggests rather that voluntary monitoring of concentrations of NTA in the environment will be a sufficient safeguard is not enough. One reason the Canadians may not have found environmental problems is that they, too, generally took the approach that monitoring for low concentrations of NTA would be sufficient. In few, if any cases, did they actually study specific areas before and after NTA introduction to assess the effects of NTA on such organisms as live in streams, lakes and rivers. Only if this is done can we be certain of environmental acceptability of NTA. In view of the quantities likely to be used throughout the United States much more caution is needed. I urge a closer adherence to the IJC recommendations.

Sincerely,

Joseph Shapiro

Mr. MAGUIRE. You will note that it refers to discussions in 1979, but suggests that a number of concerns that were expressed at that time have not found their way into the letter sent to Procter & Gamble. He finds that surprising.

He also emphasizes that specific studies should be conducted. In one paragraph in particular he says this:

It is my opinion that the EPA letter to Procter and Gamble which does not require studies but suggests rather that voluntary monitoring of concentrations of NTA in the environment will be a sufficient safeguard is not enough. One reason the Canadians may not have found environmental problems is that they, too, generally took the approach that monitoring for low concentrations of NTA would be sufficient. In few, if any, cases did they actually study specific areas before and after NTA introduction to assess the effects of NTA on such organisms as live in streams, lakes and rivers. Only if this is done can we be certain of environmental acceptability of NTA. In view of the quantities likely to be used throughout the United States much more caution is needed.

He concludes by saying that he urges a closer adherence to the IJC recommendations.

Would you agree with what he has said in that paragraph, Mr. Throdahl?

Mr. THRODAHL. May I consult for a moment?

[Mr. Throdahl and Dr. Wilson confer.]

Mr. THRODAHL. Consulting with Dr. Wilson, he says indeed we should be carrying out such tests but within the actual field conditions rather than under larger laboratory simulations. I guess that is the only way I can react to it, not having thought about it before I saw this letter.

Mr. MAGUIRE. But you would generally embrace the thrust of the paragraph; is that correct?

Mr. THRODAHL. I would think so.

Mr. MAGUIRE. The conclusion, of course, is that only if this is done and only when this is done can we be certain of environmental acceptability of NTA. That is quite in contrast to what you said on page 3.

Mr. THRODAHL. No. I was not aware of this letter obviously. I am not specifically familiar with the details of the report in question. I would like to consult my associates on that point.

It seems to me he says he urges closer adherence to the recommendations. We would like to reflect on it and come back to you as we may.

Mr. MAGUIRE. In any case, if you generally agree with the thrust of what he has said is necessary, that it becomes very difficult to conclude, as you do on page 3, that NTA presents no threat whatsoever to the environment.

Mr. THRODAHL. The document itself, which I believe you are referring to, suggests on page 3, second paragraph, "The task force recommends that NTA should not be prohibited from use as a detergent builder. The task force further recommends that its use"—and "its" is NTA—"be accompanied by studies to address the following questions." Then they suggest nine of them.

Mr. MAGUIRE. My only problem here is with your flat statement at the bottom of page 3 that NTA "presents no threat whatsoever to the environment." Among the sources that you cite as a basis for that conclusion is the task force report headed up by Dr. Shapiro. We now have his comments on this. He says quite clearly that we cannot at the present moment be certain of the environmental

acceptability of NTA until this process which the task force has recommended has in fact been carried out.

Mr. THRODAHL. These are judgmental decisions, obviously, on the basis of whether information is significant or insignificant. When you total it all up, we would conclude that, even without these admonitions, we would be doing extensive monitoring. Beyond that, it is an interpretation of whether something is insignificant. On the basis of everything we have seen to this point, we do not believe there is significant information of any kind which would suggest that NTA is not safe.

Again, you find numbers that will go into further and further minutia and refinements of minutia, and possibly we will have to examine what Dr. Shapiro proposes in more depth than we have. However, based on what we know now, we would still stay with our conclusion.

Mr. MAGUIRE. The crux of his comments here—and I take it from what Dr. Wilson just said to you which you passed on to the committee about the studies in the actual situation—I assume, therefore, that you would agree that monitoring is not enough. Is that correct?

Mr. THRODAHL. I will have to yield. I just cannot answer that question yes or no.

Mr. MAGUIRE. Can Dr. Wilson answer that question?

Mr. WILSON. I believe that Dr. Shapiro's opinion as expressed in the letter probably reflected his own opinion and not necessarily that of the panel. It certainly is a stronger statement than the Research Advisory Board made to the International Joint Commission in July 1977.

The question that monitoring is not enough, I think is appropriate and it is certainly a policy of Monsanto that significant questions that are raised by any responsible party concerning the environmental or human safety of one of our products be investigated as they arise.

In this particular case, it is our opinion that Dr. Shapiro has raised an interesting question. We believe that the probability of serious harm is very small. I think he would agree with that.

As part of our social responsibility, we would carry out appropriate investigations that would address his point without necessarily agreeing that it does constitute a threat to the environment.

Mr. MAGUIRE. I am not quite sure, having listened to you, whether you think monitoring is enough or whether monitoring is not enough. Can you just clarify that point?

Dr. WILSON. Under some circumstances monitoring is enough.

Mr. MAGUIRE. But under other circumstances it is not enough?

Dr. WILSON. Under some circumstances it might conceivably not be enough.

Mr. MAGUIRE. Which do you think the instant case before us is?

Dr. WILSON. In this particular case, I believe that monitoring is enough.

Mr. MAGUIRE. In spite of the fact that Mr. Throdahl passed onto the committee your advice that you thought additional studies would be advisable or required? Why don't you tell us yourself what it was that you would like to say on that?

Dr. WILSON. I said essentially what I have just phrased to you before. It is worthwhile to study those matters that he proposes, that the task force in its report proposed be studied, those that have not already been answered.

Mr. MAGUIRE. You are now proposing that we are going to study whether or not to do the studies?

Dr. WILSON. I am saying that most of those experiments which the task force recommended are worthwhile questions to address and find answers to. However, I do not think that not having answered them vitiates our conclusion that NTA presents no threat to the environment.

Mr. MAGUIRE. That is internally consistent. You finally got there.

Mr. Krumrei, do you have a comment on that?

Mr. KRUMREI. Yes, sir. Mr. Winters has been doing some work for our company.

Mr. WINTERS. Regarding the monitoring in Canada, there was not monitoring prior to introduction of NTA. However, the system was monitored while there was a substantial change in the average level of NTA in Canada from 6 to 15. Nothing was seen to change when the monitoring was occurring.

Mr. MAGUIRE. What was from 6 to 15?

Mr. WINTERS. The average percentage of NTA in the detergent products in Canada. There was a change from 6 to 15 percent during that 10-year period. Even the levels of NTA in environmental waters was found not to change.

In terms of monitoring aquatic species, this can really only be done to any extent in a laboratory prior to and then after you have dosed them or introduced them to NTA. Out in the environment this is just a very, very difficult thing to try to attempt.

Each one of the recommendations of the LJC and our response to those recommendations, as reflected in the EPA report, is included in the material which is handed to you and submitted to you in the booklets.

Mr. MAGUIRE. Mr. Krumrei, we had a discussion a bit earlier about whether the Joint Commission had approved in some formal sense or not the use of NTA detergents. I do not want to go back over that discussion. The record will show that is a word which at least they did not use.

However, they do include the following statement in the preface of the report on health effects of NTA, a report prepared by the United States-Canadian Joint Commission. They say:

"It is our feeling that the decision on the use of NTA must be based on societal interests rather than depending solely on scientific considerations." Would you agree with that?

Mr. KRUMREI. I think that is the point we have been trying to make, Mr. Chairman. We believe this is in the societal interest to use NTA in order to reduce the cost, as Mr. Pepper pointed out earlier, to people in nonphosphate areas, to allow those people, as Dr. Lehne has pointed out, to get the clothes as clean as they want to get them at a reduced cost.

Mr. MAGUIRE. On the question of cost, I have a memorandum dated March 11, 1980, of discussions between EPA, Procter & Gamble, and Monsanto in which Procter & Gamble is said to have

stated that NTA is more expensive to use than phosphates and much more expensive than other builders.

Mr. KRUMREI. Yes, sir.

Mr. MAGUIRE. Is that correct?

Mr. KRUMREI. That is correct.

Mr. MAGUIRE. But you just made a reference a moment ago to "more cheaply."

Mr. KRUMREI. As Mr. Pepper pointed out earlier in his statement, in an attempt to get clothes clean—and I believe Dr. Lehne corroborated that statement—people will use more detergents. They will use bleach, laundry aids, and so forth. That adds appreciably to the cost.

Mr. PEPPER. I would like to expand on that. Let me try to explain the subject you are trying to get at.

You are right that NTA is more expensive than phosphate and quite a bit more than other builders except for citrate. Let me step back a minute and just talk for a bit about how phosphate and nonphosphate products perform and where NTA fits into that, if that is all right with you.

Mr. MAGUIRE. If it is reasonably brief, yes.

Mr. PEPPER. To put this in perspective, the products we have heard about before with no phosphate—and we market them in about 20 percent of the country—

Mr. MAGUIRE. What do you use in those formulations, by the way?

Mr. PEPPER. We use sodium carbonate in most of them. We have recently introduced in some of our formulas a new and somewhat better builder called alumino-silicate or zeolite. We have been getting experience over the past year and a half with that.

Now these nonphosphate products that are out there, particularly in the zero phosphates areas, are not bad products. People are getting clothes clean to a reasonable degree with them.

I would also make the comment to you that this is highly individual subject as far as what needs and desires consumers have in their laundry and what product they choose. There are some people, though not too many, who even where phosphate products are available will choose a no-phosphate formula.

Having said that, I need to try to convey to you the fact that the phosphate formulas that we use and the formulas that would be available with NTA are substantially better than nonphosphate products. In terms of the majority of consumers, they are much preferred.

Mr. MAGUIRE. Is that true for all types of water or mainly for hard water?

Mr. PEPPER. That would be true in all kinds of water in terms of the preference of these products. It is particularly true in hard water, a little bit less true than that in medium water.

Let me go on and give you some perspective on what backs that up and why I say that about the consumer acceptance of these two forms of products.

In 80 percent of the country phosphate detergents are allowed by law. In those areas of the country there are both phosphate and nonphosphate products. In those areas of the country about 9 out of 10 or really 19 out of 20 boxes of detergent that are sold contain

phosphates despite the fact that there has been over the years a number of nonphosphate products that have been introduced and marketed. Clearly the market is telling us there that over time consumers are preferring the products that we know to clean better.

Mr. MAGUIRE. Either that or you have an extraordinarily effective advertising approach to the market.

Mr. PEPPER. That alone would be totally inconsistent, Mr. Maguire, with our experience. If we do not have a product that works well, it does not matter how good our advertising is or how much money we spend. We may do well for a short while, but we are going to be going downhill pretty quickly.

Mr. MAGUIRE. The two factors do interrelate.

Mr. PEPPER. They interrelate. My only point was that you have to have the products just to have that kind of a position.

Second, we look closely, as you would expect, at consumer mail, mail that is commenting positively on a product and some mail that is saying there is something wrong with it. In the 80 percent of the country where phosphate detergents are used we get more positive comments than we get negative comments. In the 20 percent of the country where we can only use nonphosphate detergents we get eight times as many negative comments as we get positive comments, even though our detergents are quite competitive with the market and we are trying to make them as good as we can.

My last point on this gets to the economics that I talked about in my opening statement. An individual is going to end up finally with a piece of clothing that is good enough to wear. Women are not going to have children going to school with what is a dirty shirt on their backs. If we do not provide a detergent that does a good enough job to their standards, then we have found that consumers will use bleach, they will use hotter water, and they will use other additives to get that level of performance.

In fact, in nonphosphate areas our research shows that people are using hotter water than in those areas where phosphate detergents are sold. In fact, about 25 percent more women in those areas use hot water than they do in areas where the better phosphate detergents are sold.

We know they use more bleach in nonphosphate areas because the detergents are not quite as good. About 30 percent use more bleach.

If you add all this together, we estimate that consumers in nonphosphate areas are spending in the range—and this gets back to the water hardness issue you raised—between \$20 and \$60 a year more than consumers in phosphate areas are because of these extra steps and adjustments they are taking.

That comes back to the reason we have been looking for NTA and hoping we could use it, and indeed looking for things other than NTA because we have been very much aware of the controversy on this subject and the uncertainty it represents.

Mr. MAGUIRE. Do you have anything else coming along, by the way?

Mr. PEPPER. I wish I could tell you that we did. We have other things that are hopes, but I just could not tell you today that we

have anything that approaches phosphate or NTA as an effective builder.

Mr. MAGUIRE. Let's assume that at some degree at the margin NTA as a detergent builder has at least some characteristics which may be superior to other detergent builders, at least in some kinds of water. Let's assume that.

Mr. PEPPER. That is not an issue. That is a fact.

Mr. MAGUIRE. Then the question is, if you are going to conduct a risk-benefit analysis to make a societal decision, what are the elements that go into that? In this case it looks to me as if the benefits that your statement indicates are analyzed in terms of cleaning effectiveness.

Mr. PEPPER. And cost, \$30 a household against about 15 or 20 million households. That is a half a billion dollars a year the consumers are spending.

Mr. MAGUIRE. Let's assume that is correct. On the other hand, risks have to be analyzed in this case in terms of adverse health and environmental effects or potential adverse health and environmental effects. At that point does it seem conservative, cautious, sensible, and prudent to move to an alternative, even if there is some slight or even significant loss of cleaning effectiveness as long, as you say, people are getting their clothes clean with your carbonate products or Dr. Lehne's carbonate products? Does it make sense then to move to what is known to be a safe and effective alternative rather than to put a billion pounds of material which has been shown scientifically to be carcinogenic in animals into the water supply and a carcinogenicity which is not fully understood by scientists, either in terms of its mechanism or operation, which they indicated in all the studies we have all looked at, or in terms possibly of its differential impact on subgroups in the population, say somebody who has kidney disease.

Under those circumstances does it really make sense for us not to be prudent?

Mr. PEPPER. Mr. Maguire, I understand your question. Let me say very clearly, if there were any doubt in our minds about this representing a health hazard, we would not even think about it.

Mr. MAGUIRE. There are only certain things, Mr. Pepper, that cause cancer in laboratory animals. There are very few compounds or substances that cause cancer in laboratory animals. Why should we not be especially prudent with respect to those when there is so much that we do not understand about how carcinogenesis works or whether there are cocarcinogenic effects that have not even been identified, or whether there are subgroups in the population more affected than others?

Mr. PEPPER. Mr. Maguire, the reason we have reached that conclusion is really as simple as the conviction that a "safe" threshold level has been established hundreds of thousands of times above that which would be in the environment as a result of its use in detergents. That has been agreed to within the last 3 months by the Netherlands Government which shares that view. I know there is controversy on it, but that is our conviction. We have to go by our conviction, and we are not alone on this issue in terms of the people who support it.

Mr. MAGUIRE. In a situation in which there are people with differing views on that point, there are people who do not share your conviction, people who are qualified and thoughtful—and some of them have testified here today, including the Director of the National Institute of Environmental Health Sciences—in a situation such as that where your conviction is not necessarily shared by others and where there is so much, admittedly, on all sides that is not fully understood, why would you not choose to be prudent?

If you choose not to be and you are fully confident of your conclusions, which I think is more than most of us can be most of the time, why would you not as the custodians of the public interest at least adopt a policy of prudence? That is generally the approach that public institutions and scientific institutions charged with investigating these things have taken with respect to substances which are known to cause cancer. Why would you not do that?

Mr. PEPPER. We are convinced it is safe. We went to the EPA on this issue for a review of the matter. Mr. Maguire, we are being prudent.

We recognize that, no matter what our views—and we have been developing them with research and testing over 10 years—we are not going to be able and do not intend to use this material until we are successful, and we can only do part of it, in getting what we feel to be the truth on this subject across.

Mr. MAGUIRE. On page 3 of Mr. Krumrei's testimony it is stated that "NTA exhibits no cocarcinogenic properties." We discussed that earlier. That relates to a couple of tests with a couple of other compounds.

It is stated that "NTA is not a mutagen." Dr. Rall says he does not know whether or not NTA is a mutagen.

It is stated on page 3 that NTA "does not mobilize heavy metals." Dr. Perry was here, and he told us that there was a serious question and problem about the transportation of metals.

It is stated on page 3 by Mr. Krumrei that NTA "exhibits no buildup in surface or groundwaters." Clearly from the testimony we have had and the scientific material that you, yourselves, have reviewed, there are questions about the differential likelihood of buildups in different kinds of water.

It is stated on page 3 that NTA "does not adversely affect sewage treatment." We have had informed scientific witnesses this morning who have said that in water used in sewage treatment facilities and reused that the questions have not been answered.

We are told on page 3 that NTA "does not accumulate in fish" and that "it has extremely low toxicity to fish, algae, or other aquatic species." We have been told here by experts on those subjects that the questions have not been answered.

It says on page 3 that it is biodegradable both as a sodium salt and as a complex with metals. The testimony we have had says that it depends on the real context in which we are looking at the NTA, how rapidly it is biodegraded and whether or not it builds up.

How can this committee, which is charged with oversight here, and the EPA or you go ahead under the circumstances of disagree-

ment among qualified scientists about something that everybody agrees—you agree, EPA agrees, I agree that the scientific data shows that this thing causes cancer—how under those circumstances can we put a billion pounds of it into the groundwater of the United States and then come back here 5 or 10 years from now and say, "Well, gee whiz, we really didn't understand how this was going to impact on the environment and on people's health. If we had known more at the time, back in June of 1980, we would certainly have made sure that we did not put a known cancer-causing substance into the water supply for human consumption in this country. Isn't that the issue, Mr. Pepper?"

Mr. PEPPER. I think we are going to start repeating ourselves, Mr. Maguire.

I can agree that I have felt it is right to go ahead because of the conviction that this is safe, that there is this threshold level.

Mr. MAGUIRE. What threshold level?

Mr. PEPPER. The threshold level below which—

Mr. MAGUIRE. It has not been defined. The Director of NIEHS says that we do not have the scientific data to define a threshold level. He said that today. Did you hear him say that?

Mr. PEPPER. He said he wasn't certain. That is what I heard him say. He thought there was a reasonable possibility there was, but he wasn't certain.

Mr. MAGUIRE. He said there might be a threshold somewhere but he didn't know where it was. He did not know anybody who could tell us where it was.

How can you tell us where it was? How can you be confident that you can tell us and 200 million people in the United States that you are so confident that you can tell us where it is and put a billion pounds of cancer-causing materials into the water supply? How can you be that confident, Mr. Pepper?

Mr. PEPPER. It is a conviction in the quality of the research you are running.

Mr. MAGUIRE. What is the threshold? Give us a scientific statement as to what the threshold is that we can guarantee to people who drink the water and use the detergent that they are going to be kept safe and not harmed by this material.

Mr. WINTERS. May I answer that, Mr. Chairman?

Mr. MAGUIRE. I would be delighted for anyone to answer that. I doubt that you can because our review of the literature suggests that there is not an answer that clearly specifies a level and/or that qualified scientists can agree about. Please try to answer it if you can.

Mr. WINTERS. 0.03 percent in a rodent's diet is a no-effect threshold level for NTA toxicity and carcinogenicity, according to all the work that we have completed. It does have a threshold, below that level no toxicity. Without that toxicity, no cancer. That is consistent with the NCI research work.

Mr. MAGUIRE. That is not consistent with the state of knowledge about how extrapolations are made, with the scientific uncertainty about thresholds, about cocarcinogenic effects, and about subgroups in the population, concentrations of the material itself which may vary in different types of water under different circumstances.

Mr. WINTERS. Sir, those techniques are only useful if you assume a one-hit model for cancer—that is, that you have a material that interferes directly with the cell. NTA does not, clearly does not. It is not a mutagen. Dr. Rall has indicated this in his report. It is not a mutagen. This is a specific case and you cannot discuss it in generalities from the knowledge that we have.

It does exhibit a threshold, so it does not present a cancer risk at lower levels.

Mr. MOFFETT. Would the gentleman yield?

Mr. MAGUIRE. In just a minute.

It exhibits a threshold only in the sense that laboratory tests with animals can be helpful. It is clear they can be helpful to us in signaling danger. That is the best method that we have of signaling danger.

However, neither you nor anyone else is in a position to tell the American people that your extrapolations to human populations are going to be correct or are going to prevent cancer. In fact, I have to ask you whether you can sit there and with confidence tell us that, even though this is a cancer-causing substance—and, by the way, the scientists have told us the mechanism is not understood. You tell us that you understand the mechanism but you are one of the few people that seems to understand it.

Mr. WINTERS. We are one of the few people that have worked on it for 4 years.

Mr. MAGUIRE. Therefore, you understand the mechanism of how it works?

Mr. WINTERS. Yes, sir.

Mr. MAGUIRE. I yield to the gentleman from Connecticut.

Mr. MOFFETT. I would ask about Dr. Perry's figures that I cited earlier of 300 parts per billion and possibly 3,000 parts per billion—you may recall my citing those figures. He said after a typical dilution of 8-to-1 average surface water he would anticipate NTA levels around 300 parts per billion. Then he said,

If the same range of degradation occurred in Canada, the maximum surface water concentration would exceed this by a factor of 10, making a level of about 3 ppm or 3,000 ppb. The consequences of such a situation have not been evaluated.

What about that?

Mr. WINTERS. I am aware of Dr. Perry's work. He has done some pilot plant experiments, which is always the best starting point to predict anything. However, the laboratory is the starting point. We have already done the environmental test the true test in Canada, and it just does not exist in Canada that way. That means that scientifically in the laboratory we cannot think of everything that gives us that system. The system, though, is the answer that we are trying to get after. We have already run that experiment.

Mr. MOFFETT. Have you done a real sewage treatment plant experiment?

Mr. WINTERS. Oh, yes.

Mr. MOFFETT. It seemed to me Dr. Perry was admitting what you said, acknowledging that.

Mr. WINTERS. That has been done in the Canadian operation, influent and effluent from sewage treatment, river water, drinking water, lakes.

Mr. MOFFETT. Mr. Chairman, I would ask that Dr. Perry be brought up to answer this. He is here. I think it would be useful. I do not want to prolong this, but I think it would be useful to answer this question.

Mr. WINTERS. By the way, I could add one more thing. EPA did have his information in their assessment.

Mr. MOFFETT. Would you just respond for us, Dr. Perry?

Dr. PERRY. The data I used there were the data of Canada, assuming 80 percent biodegradation of NTA. The calculation that I made was the levels of NTA which would occur in the River Thames in London, assuming an 8-to-1 dilution, which is very, very different from the phenomenal dilutions that occur in Canada. The data used is based upon the Canadian experience.

Mr. MOFFETT. Do you want to respond to that?

Mr. WINTERS. Yes. I could add one more piece of data. As you heard before, there are somewhere between 10 and 13 million pounds of NTA in the United States currently that is introduced into our waters. I think that you will find the parts-per-billion levels in river waters in the United States in the areas that we already have looked at, that is in your book, are consistent with the Canadian experience. Here is data for the United States for NTA as it is already being introduced here. I think that says the model for Canada is, in fact, consistent with the United States, and the United States will be as Canada.

Mr. MOFFETT. Dr. Perry, would you respond to that, if you would like to do so?

Dr. PERRY. I find it incredible. We are talking about something completely different. NTA already in America as a detergent?

Mr. WINTERS. No, sir, but almost 15 million pounds are sold in other commercial applications all over the United States. It is already introduced into our waters. As we would expect from the modeling, you see NTA in the influent of the sewage broadly, right here in Washington, going through the sewage treatment plant, being removed, going in the effluent as it comes out, and back into the river water.

Mr. KRUMREI. I would speculate there may be some in England as well.

Dr. PERRY. May I ask one question here? The paper which I have taken the data from is by Woodiwiss, et al. This has been extensively quoted today and contains the data which I have presented for Canada. If one looks at the dilutions involved, they are typically one hundredfold and often well over a hundred. The degradation I have assumed takes place in that calculation is 80 percent, which is the Woodiwiss et al figure, Mr. Winters. If you look at the data for the individual plants, although the authors claim that you cannot relate the influent to the effluent because uncoordinated samples were taken, in reality if you assume that you can, which is not altogether unreasonable, then the variations in biodegradation range between about 17 percent and 90 percent.

In other words, there is a very variable NTA biodegradation taking place. Furthermore, if you assume you cannot do this correlation, why then did the authors use the same data to evaluate metal mobilization?

Mr. WINTERS. The only other comment that I would like to add is we have gone through exactly the same kind of theoretical calculations for Canada before we went with NTA in Canada. We, indeed, overestimated what actually turns out to be in the environment. That is the final experiment.

Mr. MOFFETT. Thank you, Mr. Chairman.

Mr. MAGUIRE. Mr. Lent?

Mr. LENT. Thank you, Mr. Chairman.

To try to put this discussion into perspective, none of these firms are using NTA currently in their detergent products. They are abiding by an order or a decision back in 1970 or they made a voluntary decision, in either case, to remove NTA from their detergent products. Even today none of them are using NTA in their detergent products, but they have come to our Government and asked our Government if they can use it. Our Government, through the mechanism of the EPA, which is the statutory organization that is charged with responsibility in this particular field, has told them, yes, you can use it.

I have some qualms about the methodology of oversight here where we are not really questioning the agency of our Government, at least not yet but maybe they are the next panel, for making this decision. However, we seem to be leaning on the industry, which is just waiting for a decision and which has waited for 10 years and now finally has this letter from EPA dated May 27.

A few moments ago, Mr. Chairman, you introduced into the record a letter from Joseph Shapiro, who was the Chairman of the International Joint Commission. I assume by introducing this into the record you accept the fact that Mr. Shapiro is an authority in this particular field, NTA.

If you will look at the first paragraph of his statement, he says, "As we stated in the IJC report, use of NTA does not appear to constitute an environmental hazard."

Then in the last sentence he says, "I urge a closer adherence to the IJC recommendations."

We should not lose sight of the fact that the IJC recommendation was that NTA should be permitted to be used as a detergent builder. That was the conclusion.

The only thing we are quarreling about or quibbling about with the Shapiro letter—and I am sure these gentlemen who want to go into the NTA business are fully in accord with the conclusion of the IJC—is whether or not there ought to be monitoring and to what extent that monitoring ought to take place.

As I read the letter of May 27, 1980, from the EPA to Procter & Gamble, which is referred to by Mr. Shapiro in his letter, they indicate that "Manufacturers should conduct monitoring and environmental studies to confirm the predictions of low environmental levels during the initial years of resumed use. EPA would like to review the design of such studies."

As I read these documents, you have an arm of the U.S. Government saying, "Go ahead and use it, provided you conduct monitoring and environmental studies."

Mr. PEPPER. Mr. Lent, I might be able to be of help in wrapping this up. Before we had heard anything back from EPA or EPA took their position, we had already reached the decision we were going

to conduct monitoring studies on this as it comes in. We doubt if it is going to show anything much different than Canada, but that is something that we plan to do and would do if we do proceed to use this material. That is not at issue.

Mr. LENT. The only thing we are really quibbling about is this first sentence of the second paragraph of Dr. Shapiro's letter where he says, "It is my opinion that the EPA letter to Procter & Gamble which does not require such studies"—as I read the EPA letter, it does require such studies, not just monitoring.

Mr. PEPPER. Whether it does or not, we are going to do them.

Mr. LENT. The premise upon which Dr. Shapiro's letter is based appears to me to be in error or perhaps he did not have available in front of him the Procter & Gamble letter at the time he made this telephone call to a representative of the subcommittee staff who typed this letter. Nonetheless, the letter to Procter & Gamble is very clear. I have it in front of me.

Manufacturers should conduct monitoring and environmental studies to confirm the predictions of low environmental levels during the initial years of resumed use.

Certainly the big picture of Dr. Shapiro as incorporated in the IJC study, on which he worked for years—it is a big, fat thing, if anybody wants to read it—the bottom line in the recommendation is that NTA should be permitted to be used as a builder for detergents. If we are going to introduce this letter in evidence, then it can be used to substantiate the EPA letter as well as to detract from it.

Mr. KRUMREI. May I respond, Mr. Chairman?

Mr. MAGUIRE. I do not know if he asked you a question.

Mr. LENT. I would be happy to have an answer or response.

Mr. KRUMREI. I would just want to amplify Mr. Pepper's comment. We do intend to monitor. We intend to share with and get the advice of EPA on the protocol to be used. We intend to share all of the data with them, so that they will be fully conversant with what we are finding at the time we are finding it. We have no other plans other than that.

Mr. LENT. I thank the chairman for introducing Dr. Shapiro's letter because I think it firms up the EPA decision and supports it. His bottom paragraph is he urges "a closer adherence to the IJC recommendations."

When I then turn to the IJC, it says in effect that NTA should be permitted to be used as a builder in laundry detergents. Is that correct? If I am incorrect, straighten me out.

Mr. MAGUIRE. Has the gentleman completed his questioning.

Mr. LENT. It is really a question of you.

Mr. MAGUIRE. I included the entire text of the Shapiro letter.

Mr. LENT. OK.

Mr. MOFFETT. Would the chairman yield briefly on this point?

Mr. MAGUIRE. Yes.

Mr. MOFFETT. Unfortunately, the gentleman from New York only read part of that sentence in the letter because I am sure it suited his case, and we all tend to do that. He stopped after saying, "use of NTA does not appear to constitute an environmental hazard." The sentence, of course, goes on to say, "but because use in the United States would be on a much greater scale than hitherto we

felt that its use here should be accompanied by specific studies to address the expressed concern."

Then, as the gentleman noted, in the last sentence Dr. Shapiro says, "I urge a closer adherence to the IJC recommendations." I would only suggest that this can be read in a number of ways. If you read, as I am sure the gentleman from New York has, the conclusions and recommendations of the IJC, they do in fact say—and the gentleman is correct on this—"based on this conclusion the task force recommends that NTA should not be prohibited from use as a detergent builder."

They then go on and take well over two pages talking about the things that we do not know regarding NTA. I am just saying it is at least arguable that what Dr. Shapiro is getting at here is that in urging closer adherence to the IJC recommendations is that these studies be carried out. I would submit to the gentleman that we do not have evidence that that has been done within Government prior to this EPA decision.

Mr. LENT. The gentleman would agree that, had Dr. Shapiro been invited here as a witness—and perhaps he should have been—he would have backed the IJC study.

Mr. MOFFETT. We cannot speculate on that.

Mr. MAGUIRE. If the gentleman would withhold, it is very hazardous, indeed, for him to attribute statements to Dr. Shapiro that he believes Dr. Shapiro might have made had he appeared before the committee. He was invited to appear. He had other commitments and was not able to appear.

The gentleman is welcome to his own interpretations of any material before the committee, but I will have to say on behalf of Dr. Shapiro or anyone else who is not testifying here today that imputations by the gentleman as to what they might have said had they testified are clearly out of order.

Mr. LENT. I do not think it is out of order for me to read the document. I have read it very carefully.

Mr. MAGUIRE. You are perfectly in order to read the document.

Mr. LENT. The gentleman from Connecticut has read even the rest of the sentence which says, "we felt that its use here"—"use" meaning NTA's use—"should be accompanied by specific studies to address the expressed concern."

Dr. Shapiro's position is very positive that NTA should be permitted to be used as a detergent builder provided these follow-up studies are made.

Mr. MAGUIRE. I can only say to the gentleman that I am delighted that he and I share an affection for the Shapiro letter.

Mr. LENT. But we seem to come to differing conclusions from reading it.

Mr. MAGUIRE. I think it is reasonably clear to everyone that that is in fact the case.

Mr. MOFFETT. Gentlemen, you have been very patient. We appreciate that.

Going back to this figure of I think it was \$30 a household—

Mr. PEPPER. That is the average.

Mr. MAGUIRE. Where does that come from? Could you tell us something about where you come up with that kind of figure? Is

that a figure that reflects what people are paying now because we are not using NTA?

Mr. PEPPER. Yes. That is the figure. I do not have all the details on it. It includes usage studies which show percentage of washloads, for example, that contain bleach, the percentage of washloads which contain a laundry additive, the percentage of washloads which run in hot, cold, or warm water among a broad base of the population.

Mr. MOFFETT. Where do you get that?

Mr. PEPPER. I cannot comment on the specific study. We would generally send out questionnaires. Usually it is a diary study where we will send out through the mail a questionnaire which will ask consumers to mark down on a diary basis each washload, what setting on your washing machine did you use, what products did you use in addition to a detergent.

With that then we just applied the incidence of the usage of different additives in the different areas, those with phosphate detergents and those in which phosphate detergents are not allowed. We took the cost of bleach or the cost of hot water relative to cold water and applied those.

Mr. MOFFETT. When you come out with a figure such as that it obviously has an impact.

Mr. PEPPER. I hope it does. It has a big one on us.

Mr. MOFFETT. Before I embrace it, I want to have some idea of how it is put together.

Mr. PEPPER. Mr. Moffett, we would be delighted to submit for the record a detailed explanation and a categorization of each of the individual costs that make it up.

Mr. MOFFETT. I would like to see that.

[Testimony resumes on p. 139].

[The following material was received for the record:]

Consumer Costs Associated WithDetergent Phosphate Bans

This provides additional information concerning the added ~ \$20-\$50 per year costs relate to the home laundering process incurred by households in areas which ban the use of phosphates in laundry detergents. This information details cost factors noted by Mr. John E. Pepper of The Procter & Gamble Company in his testimony to the House Committee on Interstate and Foreign Commerce, Oversight and Investigations Subcommittee during their hearing on sodium nitrilotriacetate (NTA) June 26, 1980.

The bases for the cost figures provided are Procter & Gamble consumer and market research, and an evaluation of these costs by the Soap & Detergent Association (SDA), 475 Park Avenue South, New York, New York¹ of which we are a member. The SDA documented the details of these costs in terms of 1978 dollars, and are therefore, conservative given the current rate of inflation. We have roughly estimated these costs in terms of 1980 dollars in this attachment.

The costs incurred by consumers in areas banning the use of phosphates in laundry detergents can be grouped in two general categories: (i) adjustments in laundering habits and practices to compensate for the poorer performance of non-phosphate laundry detergents, and (ii) damage to garments and washing machines from laundry detergents utilizing sodium carbonate as a primary builder material. A more detailed discussion of these two cost groupings is provided below.

Costs Associated with Adjustments in Laundering Habits and Practices

Non-phosphate laundry detergents provide poorer overall cleaning performance than

products which contain a low level of phosphates (current average range of phosphorus by weight in laundry detergents containing phosphates is 6 to 7%). Consumers make adjustments in their laundering habits and practices when phosphates are banned from use in laundry detergents in an attempt to regain the level of cleaning performance provided by the traditional phosphate products. Market survey and consumer monitoring studies have shown these adjustments involve increased use of detergents, laundry aids such as pretreatment products, fabric softeners and bleach, and more hot water. Since the retail cost of non-phosphate and phosphate laundry detergents are equivalent, these adjustments result in increased costs for the home laundering process.

One market survey study³ provided a comparison of laundry product sales in grocery stores in Indianapolis, Indiana (phosphate ban area) with three Ohio cities having no detergent phosphate legislation. The change in product case sales was compared for the three years after enactment of a ban to the two years prior to the ban (base period). The relative change between the two areas served as the final comparison, with each area's pre-ban period serving as the base comparison. This avoided variables other than the effect of the ban. The results of this study showed that the sales of detergents and laundering aids increased at a faster rate in Indianapolis than in the Ohio cities all three years monitored after a ban was enacted in Indiana. The following table, based on results of this study, shows the annual increased cost to households in ban areas related to the purchase of extra laundry detergent and laundry aids.

Extra Annual Cost Per
Household in Ban-Area versus Non-Ban Area

<u>Product Category</u>	<u>Adjusted 1980* Dollars</u>
Detergents	\$2.42
Liquid Bleach	.70
Dry Bleach	.46
Fabric Softener	2.26
Water Softener	.23
Total Net Increase	\$6.05

* 1980 dollar figures derived by scaling up 1975 dollars from study based on Consumer Price Index factors (Bureau of Labor Statistics), which results in 45.2% increase for this category.

Another study of a different kind conducted in 1977-1978 and reported in 1979³ also showed increased costs to consumers in phosphate-ban areas associated with adjustments in laundering habits and practices. This study involved a nationwide telephone survey conducted by an independent research firm among a statistically representative sample of households in ban areas (300 respondents) and non-ban areas (1,250 respondents). The survey was conducted throughout the year to avoid any season related bias. A variety of household laundering habits and practices were surveyed and compared. However, this type of study does not allow an accurate comparison of laundry detergent use so this factor was not compared as it was in the previously noted study. The results of this study as shown in the following table revealed differential effects in four areas: (i) use of hot water, (ii) use of bleach, (iii) use of fabric softeners, and (iv) use of pretreatment products.

<u>Laundering Practice</u>	<u>Extra Annual Cost Per Household Where Detergent Phosphate is Banned (Adjusted 1980 Dollars)†</u>
Use of hot water	\$6.59
Use of bleach	1.86
Use of fabric softener	1.83
Use of pretreatment	.28
Total	\$10.56

† Costs of bleach, fabric softener and pretreatment based on 1979 retail cost of market leaders in product category and updated to 1980 dollars via Consumer Price Index factors. Hot water costs based on Department of Energy data estimating clothes washer temperature settings and average kilowatt per hour cost.

Utilizing the lower of the costs obtained in the two surveys for bleach and fabric softener allows a conservative estimate of the increased cost to households in phosphate-ban areas associated with adjustments in laundering habits and practices.

<u>Category</u>	<u>Adjusted 1980 Dollars</u>
Laundry Detergent	\$2.42
Bleach	1.16
Fabric Softener	1.83
Water Conditioner	.33
Pretreater	.28
	Subtotal \$5.92
Energy (Hot Water)	6.59
	Total \$12.51

These studies indicate the average increased cost to households in phosphate ban areas associated with adjustments made to improve laundering performance is \$12.51 per year.

Costs Associated with the Adverse Effects of Carbonates

Due to availability and cost, sodium carbonate has served as the principal alternative builder material to phosphate for granular laundry detergents in areas which ban phosphate use. Sodium carbonate performs the primary builder function (binding mineral hardness ions principally calcium and magnesium) in a manner different than phosphate or NTA. It combines with mineral hardness ions to form insoluble precipitates; whereas phosphate or NTA binds with mineral hardness ions and holds them in solution. The use of carbonates in non-phosphate detergents results in precipitates on garments and in washing machines not seen with

phosphate detergents. The magnitude of the precipitation is primarily dependent on the level of sodium carbonate used in the product and the mineral hardness of the wash water. As either increases, the amount of precipitation increases.

The calcium carbonate precipitates have been shown to decrease the wearable life of garments,^{4,5} and damage washing machine parts.^{6,7} Both of these adverse effects result in sizeable consumer costs.

Based on U.S. Census Bureau and National Conference Board data, annual U.S. expenditures on washable garments total about \$344 per household per year. The above noted studies^{4,5} when adjusted for the typical carbonate content of laundry detergents in phosphate-ban areas indicate that a 0.04% reduction in wearlife occurs for each part per million (ppm) of water hardness.¹ The cost per household due to decreased garment wearlife can be calculated as follows:

$$\frac{0.04\% \text{ reduction/ppm water hardness}}{100\%} \times \$344/\text{family/year} \times \text{Mineral Hardness of Water Supply, ppm as CaCO}_3$$

A representative median water hardness for the four major water hardness classifications; soft, medium-hard, hard and very hard would be 30, 90, 150 and 210 parts per million respectively. Carbonate-based laundry detergents account for approximately a 56% greater portion of the market in phosphate ban areas than non-ban areas. Adjusting for this factor and use of the formula above shows the average increased clothing costs to households per year in ban areas due to decreased wearlife are:

<u>Soft Water</u>	<u>Medium-Hard Water</u>	<u>Hard Water</u>	<u>Very Hard Water</u>
\$3.66	\$10.96	\$18.28	\$25.59

The adverse effects of calcium carbonate precipitates have been reported to increase the frequency of service calls for washing machines and result in a shorter life for machine parts in ban areas.⁶ In the areas where these results were observed, the average water hardness was classified as hard water. Extra service call fees were based on a \$28.00 average cost for a service call,⁸ service calls normally occurring once every two years,⁸ and an increased frequency of calls of 15 to 20% in ban areas.⁶ Extra costs for replacement parts were based on an overall 15-20% shorter life for parts in ban areas⁶, an extra cost of \$137.50 for parts commonly replaced⁶, and the assumption that these costs only occur once over the 10-year design life of a washing machine. Adjusting these costs for the four major categories of water hardness, gives the following estimated average cost per year to households in non-phosphate areas due to washing machine damage related to carbonate detergents.¹

<u>Soft Water</u>	<u>Medium-Hard Water</u>	<u>Hard Water</u>	<u>Very Hard Water</u>
\$3.11	\$9.34	\$15.57	\$21.80

Use of a mechanical water softener would be expected to reduce the adverse effects of carbonate-detergents. This is a practice that has been recommended by professional Home Economists to residents in hard water areas to help compensate for a lack of phosphates in laundry detergents. However, it does not reduce total costs to these residents since the costs to rent or purchase a unit, plus operating costs, range between \$70 and \$205 per year.¹ Costs due to adjustments in laundering habits and practices would be additional to these costs.

Combining the costs for adjustments in laundering habits and practices with those due to the adverse effects of carbonates gives the total average annual household costs attributable to detergent phosphate bans. The following table presents these costs relative to water hardness of wash water.

Extra Annual Cost Per Household Where Detergent Phosphate Is Banned

Cost Component	Costs of Each Class of Water Hardness				Mechanical Water Softener
	Soft	Medium Hard	Hard	Very Hard	
Cleaning Products	5.92	5.92	5.92	5.92	5.92
Energy (Hot Water)	6.59	6.59	6.59	6.59	6.59
Washable Clothing	3.66	10.96	18.28	25.59	*
Service Calls	0.47	1.41	2.36	3.30	*
Parts Replacement	2.64	7.93	13.21	18.50	*
Mechanical Water Softener	--	--	--	--	70 - 205
Total Costs	\$19.28	\$32.81	\$46.36	\$59.90	\$82.51-217.51

* These costs are not presented since the extent to which household water softeners reduce water hardness varies depending on the operation and maintenance of the unit.

In summary, the data show that the average 1980 annual cost to consumers of a phosphate laundry detergent ban is ~\$20-\$60 per family depending on the level of water hardness. Multiplying the average cost per family having medium water hardness, \$32.81 (national average hardness is in this range), by the total number of families living in phosphate ban areas (about 15.9 million) gives a total national cost of phosphate laundry detergent bans of ~\$520 million. It should be remembered that this ~\$520 million total cost is borne by 20% of the U.S. population.

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7. R. Schuck (General Electric Company), testimony for Public Hearing on HB 882 Regarding Proposed Phosphate Ban in the State of Ohio, presented to Energy & Environment Committee, Ohio House of Representatives, March 13, 1978.
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Mr. MOFFETT. I might also say that I do not profess to be an expert on this industry. However, when we start talking about consumer costs, it is at least arguable—you can at least have a discussion and have two sides present at the discussion—that, No. 1, the industry is incredibly concentrated with Procter & Gamble being the leader, obviously, of an industry that has market dominance by three firms. There are phenomenal promotional expenditures in this industry. Again, I say it is arguable. I would never take the position that there should not be promotional expenditures, but to the tune of what—\$300 or \$400 million in T.V. advertising, if I am not mistaken, by Procter & Gamble—does that sound right?

Mr. PEPPER. I don't know.

Mr. MOFFETT. Anyway, it is a lot. You fellows are in the business so you are much more capable of speaking on it than we are, but obviously there are things which have some value in terms of the company's position—the free samples, the surprise gifts in the laundry detergent boxes, the couponing, the dissemination of the cents-off coupons, and particularly the multiplication of different brands.

I do not really need at this point a long dissertation on the differences in my wash if I use, let's say, Tide, Cheer, Bold, Gain, or Oxydol. However, from my layman's understanding, there is not one heck of a lot of difference. They are all phosphate-built anionic detergents. I think you are hard-pressed to make a case that it makes a lot of difference.

However, for marketing purposes and purposes of profit we have this tremendous differentiation and multiplication of brands. This is not a hearing on the structure of your industry, and I do not mean to make it into that, but when we start talking about cost to the consumers it is rather hard to simply focus on one thing that, as Mr. Maguire has said, could be a damaging thing. You are not convinced that it is, and I am not convinced that it is at this point, either. I do not know.

One would hope that the industry, and particularly the leaders of the industry to the extent that they can within the law, would seek to find out where we can cut other costs and get it down to a point where maybe we have to do without NTA. I do not suggest that it necessarily will.

Mr. PEPPER. I just want to take 30 seconds to assure you that there is no priority in our business today, in the detergent business—and this is really throughout Procter & Gamble—any higher than reducing the cost and controlling the cost of our product, our packaging, and our manufacturing expense, as well as our advertising and promotional expenses. It is absolutely vital to us in these times for the health of our business, quite frankly, to do that.

The amount of resources we are putting against this today in our product development activity, the critical approach we are taking to how we spend money in advertising and promotion, is simply greater today than it has ever been in my career with the company, as it well needs to be.

Mr. MOFFETT. Thank you, Mr. Chairman.

Mr. MAGUIRE. Mr. Krumrei, if EPA had not given Procter & Gamble the go-ahead to market NTA, would you have marketed the product?

Mr. KRUMREI. No; we felt we needed to talk to the agencies with whom we had the voluntary agreement in the first place to withdraw this material and get their point of view on the safety of the material at this time.

Mr. MAGUIRE. You would, of course, have been under no legal obligation to keep the product off the market.

Mr. KRUMREI. That is correct.

Mr. MAGUIRE. But you would not have marketed the product.

Mr. KRUMREI. We thought it would be prudent to talk to the people that were involved in our going off the market in the first place with this material.

Mr. MAGUIRE. Could it then be concluded that you had a vested interest in securing a favorable decision on this matter from EPA?

Mr. KRUMREI. If by vested interest you mean trying to get a better product for the consumer, yes, sir.

Mr. MAGUIRE. You clearly were not neutral with respect to the result. You really wanted an affirmative decision.

Mr. KRUMREI. We would like to have the opportunity to use almost any builder we can lay our hands on, sir, to enable us to develop the best possible product at the lowest possible cost.

Mr. MAGUIRE. Do you feel that there was any possible conflict of interest involved in the written and oral communications that you had with EPA during the time that this matter was under deliberation by EPA, given that you had a direct interest in the result?

Mr. KRUMREI. No, sir.

Mr. MAGUIRE. Or that there was any conflict of interest involved in your submitting suggested revisions and having many of them adopted by EPA?

Mr. KRUMREI. No, sir. I do not know that many of them were adopted by EPA. That is your conclusion. I have not looked at the comparison of the two.

I think there was nothing wrong or improper in our talking to EPA because, by and large, our discussions with EPA and the meeting we held that you referred to in March were to give them data so that they could better evaluate the risk assessment of the material. We did the same thing with NCI. We also did it with the National Toxicology Program Subcommittee, which also invited us to come and visit them and talk with them.

Mr. MAGUIRE. You were concerned, as the memo of March 11, 1980, indicates, about the possibility that if you introduced NTA you might be hit by EPA.

Mr. KRUMREI. Hit by what, sir?

Mr. MAGUIRE. The memo here says that Procter & Gamble was "afraid of EPA hitting them" after it is on the market, as happened in 1970. Is that your recollection of the conversation on March 11, 1980?

Mr. KRUMREI. I think we may have referred to the fact that we would prefer to let EPA know all the facts before we went to the market, give them an opportunity to make a risk assessment rather than go to the market and then make a judgment after we went to the market.

Mr. MAGUIRE. The memo prepared by Justine Welch of EPA says that Procter & Gamble indicated they "are satisfied that material is safe to use in detergents" and that they "provide a press release

for us to that effect." What press release was that?

Mr. KRUMREI. That was not a press release. It was a suggestion to the Agency of the type of memo that would be most useful to us if EPA decided that the risk assessment was finally going to be positive. It was not a press release.

Mr. MAGUIRE. You presented EPA with a draft memo of what they might say that would be most helpful to you in the event that they should make an affirmative decision?

Mr. KRUMREI. We presented a memo I had written which listed some of the things that we felt could be useful to determine the problems that we had—in other words, to delineate the problems we had.

Mr. MAGUIRE. Is that a memorandum that you could provide to the committee?

Mr. KRUMREI. Yes, I believe I can.

Mr. MAGUIRE. Do you have it with you?

Mr. KRUMREI. No, I do not. We will send it to you.

Mr. MAGUIRE. We will hold the record open, without objection, for a copy of that memorandum.

[The following material was received for the record:]

EPA ANNOUNCEMENT ON NTA

The Environmental Protection Agency today released its conclusions regarding the safety of trisodium nitrilotriacetate, more commonly known as NTA, following its review under the Toxic Substances Control Act. EPA is conducting multi-staged risk assessments for chemicals under this Act. This involves a comprehensive process to identify and evaluate risks associated with the use and the disposal of chemicals. The third stage of this process includes an extensive, in-depth review of the validity and significance of the available data.

EPA has recently completed such a third stage review for NTA, a material used in detergents in Canada, Sweden and Finland, and proposed for use in detergents in the U.S. About 10 million pounds per year of NTA are used currently in the U.S. in industrial applications. Based on this exhaustive review and evaluation of the safety information for NTA, EPA has concluded that expanded commercial use of NTA poses no unreasonable risk to human health or to the environment.

Task forces composed of U.S.-Canadian scientific experts, which were convened by the U.S.-Canadian International Joint Commission (IJC) involved with the water quality of the Great Lakes, have also recently reviewed the extensive information on the safety of NTA. On the basis of these reviews, the IJC concluded in 1978 that NTA should not be prohibited from use in detergents. The Canadian government also came to the same conclusion, and has permitted broad-scale use of NTA since 1971. EPA's comprehensive review agrees with these previous assessments and conclusions.

The use of NTA in Canada has been accompanied by monitoring programs which have shown very low concentrations of NTA in the environment. A U.S. detergent manufacturer has been monitoring the concentrations of NTA in selected geographical areas of the U.S., and has reported concentrations in drinking water of low parts per billion. Based on its evaluation of NTA and the Canadian monitoring data, EPA has concluded that expanded commercial use of NTA in the U.S. will not meaningfully affect the quality of drinking water. EPA believes it appropriate to further confirm the applicability of the Canadian data to the U.S. situation, and therefore, EPA has accepted industry's offer to undertake and report the results of a monitoring program when NTA is introduced into detergents marketed in the U.S.

NTA was used in U.S. detergents in the late 1960's, but was voluntarily withdrawn in December, 1970 by major detergent manufacturers at the request of the U.S. Surgeon General. This action was based on preliminary studies conducted by the U.S. National Institute of Environmental Health Sciences (NIEHS) indicating that teratogenic effects (birth defects) might be enhanced when high levels of NTA and high levels of certain heavy metals were injected into rats and mice. Testing completed since then has shown that these studies were not valid and that NTA causes no such effects.

In a study conducted by the National Cancer Institute (NCI), high dosages of NTA in the diet of experimental animals showed toxicity to the urinary tract. At the highest dosages tested neoplasms were the manifestation of the toxicity. No such toxic effects were observed at lower dosages. EPA has evaluated recent scientific studies concerned with the mechanisms by which NTA causes such toxic effects for purposes of making a risk assessment for expanded commercial use of NTA in the U.S. EPA has concluded that it is inappropriate

in the case of NTA to extrapolate the toxicity data from high dosages in animal studies to the extremely low levels likely to be encountered by humans. The expected level of NTA to which humans would be exposed with its expanded use, based on the Canadian monitoring programs, is about 300,000 times lower than the highest level at which NTA exerts no toxic effects in animal studies. This confirms that expanded use of NTA, including its use in detergents, poses no unreasonable risk to human health.

Mr. MAGUIRE. You said a moment ago that if EPA had not made the decision that it did, you would not have gone ahead. Isn't that correct?

Mr. KRUMREI. Yes, sir.

Mr. MAGUIRE. The memorandum by Justine Welch says the following—

Mr. LENT. I wonder if the gentleman could furnish copies of the memorandum.

Mr. KRUMREI. I have not seen that memorandum to which you refer.

Mr. MAGUIRE. I wonder if the clerk would give copies of that to the witnesses and to all members of the committee.

[The memorandum referred to follows:]

Meeting 3/11/80 with Procter and Gamble, Monsanto and Grace

Attendees

EPA: S. Jellinek, W. Muir, R. Hertz, K. Brink, J. Welch and R. Hill

Industry: Kumrei, Winters, Cowan - Procter and Gamble
Lorenzen - Grace
Throdahl - Monsanto

Procter and Gamble:

- wanted to know status of risk assessment, what our concerns and questions were.
- has supplied us all the data they have on NTA and have been talking to people at Office of Science and Technical Policy, Bob Tardiff (NAS), Paul Foley (ITC) and Canadian Government.
- say NTA also used in Sweden, Finland, Holland, (recent paper showing NTA does have a threshold for carcinogenicity was provided) Norway.
- want to use NTA to improve cleaning of nil-P detergents; market size estimated at \$400 million .
- say NTA only ingredient that comes close to substituting for all the functions of phosphates (eg. soil removal, Mg and Ca sequestering).
- say NTA more expensive to use than phosphates and much more expensive than other builders that don't work.
- have no plans at present to introduce NTA to non-P legislated areas.
- would not use a widespread advertising campaign to introduce NTA-containing products
- Monsanto says that current plant capacity would limit the amount of NTA introduced over short term; that they need big commitment for use to be able to manufacture cheaply.
- announced monitoring program to confirm that U.S. levels same as Canada; will monitor sewage influents and effluents from a variety of treatment plants, surface waters, and drinking waters they have already monitored for base-line data in Indiana, Columbus, Ohio, Washington, D.C. and have seen NTA in ppb level that results from industrial uses; have seen seven ppb as maximum in drinking water; most samples had non-detectable levels (<1 bbp)

- don't believe that use in detergents would add to background since NTA is degraded.
- have no seasonal monitoring data; began in June 1979.
- said production could go as high as 600 million pounds if used across country.
- wanted support for introduction; afraid of EPA hitting them after its on the market as in 1970.
- are satisfied that material is safe to use in detergents and provide press release for us to that effect.
- said if don't get EPA support, they are unsure of what their response will be
- said there are no patent exclusions; P&G would not have sole rights to use NTA
- said they will check for incremental increase of NTA in U.S. drinking water
- wanted to know when we would provide our judgement; they wanted it ASAP (e.g. 15 min.)

Environmental Protection Agency:

- S.J. cautioned that there are factors beyond the risk assessment that impact his answer, e.g. possible criticism for not taking action to control known carcinogen.
- told P&G that we were not in the business of endorsing chemicals, particularly known carcinogens.

Mr. MAGUIRE. Mr. Krumrei, on page 2 there is a statement midway down the page that says Procter & Gamble "said if they don't get EPA support, they are unsure of what their response will be."

Mr. KRUMREI. Yes, sir.

Mr. MAGUIRE. How does that mesh with your statement that you would not have gone ahead if the EPA had not made the decision that it made? Does that represent a conclusion that you have arrived at since the 11th of March or is this an incorrect summary of what you said on the 11th of March?

Mr. KRUMREI. It is a conclusion reached after the 11th of March but before the release of the EPA letter to me. It was an internal decision within our company as to what the potential publicity might be.

Mr. MAGUIRE. Farther down the page the memo says that Procter & Gamble "wanted to know when we"—that is, EPA—"would provide our judgment." It goes on to say, and I quote, "they wanted it as soon as possible; that is, in 15 minutes."

Mr. KRUMREI. I guess, sir, I ought to learn not to be flip. I said that with a smile.

Mr. MAGUIRE. But you did say that?

Mr. KRUMREI. It was a flip comment, yes, sir.

Mr. MAGUIRE. You did say that?

Mr. KRUMREI. Yes, sir.

Mr. MAGUIRE. Presumably you would agree that would be an inappropriate period of time to have a response from EPA.

Mr. KRUMREI. Certainly. It would be impossible for EPA to do that. That is why I said it with a smile. I will probably not ever be flip again.

Mr. MAGUIRE. Mr. Throdahl, you were at this meeting?

Mr. THRODAHL. Yes, sir.

Mr. MAGUIRE. Did you say anything at the meeting?

Mr. THRODAHL. Well, I am quoted here in terms of Monsanto says. That is a factual statement.

Mr. MAGUIRE. It says you said you would need a big commitment for use to be able to manufacture cheaply. Is that correct?

Mr. THRODAHL. That is correct.

Mr. MAGUIRE. What is the cutoff point, Mr. Throdahl or Mr. Krumrei, from the marketing point of view as to the advantage to you of switching to NTA? How big a market do you have to have to make this economically attractive to you, given that we have already established that the cost of NTA in terms of its being an ingredient in the formulation is higher than some other alternative ingredients? I am not addressing myself, obviously, now to the cost to the society in the use of energy or hot water. I am talking about the cost to the company of the ingredients.

You must have some calculations of the market performance or coverage that would be applicable.

Mr. THRODAHL. I do not run that part of the business, obviously, but let me try in general to say what the philosophy would be.

You know our current capacity. It has been reported. It is 75 million pounds each year. We could expand marginally or incrementally, as we call it, beyond that for relatively minor sums of capital. That is called debottlenecking.

However, if the approval were obtained to move forward and customers such as Procter & Gamble and others were to decide to make detergents with NTA formulated in them, obviously we do not have enough capacity. There was another man named Mr. Lorenzen from Grace. Combined there is not enough capacity in the country. That would mean new capital facilities.

Before one would invest in new capital facilities, one would have to be reasonably sure that the markets would develop. You make a risk judgment on that, admittedly.

What that statement means is that we need a big commitment, meaning if it were some multiple of 75 which was obviously reasonable, then we would have to be pretty sure that indeed that was real. As Mr. Krumrei said a few moments ago, without some kind of official statement from EPA what happened in 1970 could recur.

Mr. MAGUIRE. Therefore, there was quite a bit at stake here for you on this decision with respect to decisions that you would have to make about capital investment?

Mr. THRODAHL. Certainly. It is the normal business judgment. It is not unusual. You do this with any kind of a large investment that would amount to many millions of dollars.

Mr. MAGUIRE. Did you think there was any possible conflict of interest involved in these kinds of discussions with EPA about decisions which would affect a possible product?

Mr. THRODAHL. You see the attendees listed at the top of that memorandum. That was in front of Mr. Jellinek and his senior people. We appeared before them in a responsible way. We conducted ourselves openly. I think in every sense it was an appropriate way to do it.

Mr. MAGUIRE. Did you submit any revisions as Procter & Gamble did or any comments on any of the prepared documentation?

Mr. THRODAHL. No, we did not.

Mr. MAGUIRE. Why not?

Mr. THRODAHL. I believe we thought whatever Procter & Gamble would respond would certainly be appropriate. After all, we would supply customers such as Procter & Gamble, not the general public. They had a far more responsible role to play in that than would we. I would defer to Mr. Krumrei if he would like to comment.

Mr. MAGUIRE. In short, you have not done your own independent analysis of all of this. You have followed along after P. & G. Is that correct?

Mr. THRODAHL. No, that is not true.

Mr. MAGUIRE. That is not true?

Mr. THRODAHL. We have concentrated more, obviously, on the environmental effects and impact, but we, too, are as concerned about the safety of our workers and the ultimate safety of the people who use it. If NTA detergents were to be in the marketplace and would not be accepted by the consumers, we aren't selling NTA. Therefore, from a purely self-enlightened point of view, we would definitely want to be assured that we were doing everything that was responsible to make certain that the product was as we had represented it to be.

Mr. MAGUIRE. Mr. Krumrei, what is the tip point for you on what kind of a market you need before you go ahead with the investments required?

Mr. KRUMREI. Before we can move ahead?

Mr. MAGUIRE. Yes, to use NTA as a detergent.

Mr. KRUMREI. I will defer to Mr. Pepper on that. Just let me start the discussion by saying that we never go into a market unless we go into a small test market area to determine the consumer appeal of that particular product. I will now defer to Mr. Pepper.

Mr. MAGUIRE. I am not talking about the testing. I am talking about ultimately marketing the product on a wide scale.

Mr. PEPPER. I do not think there is the kind of tip point that you were hearing about from the Monsanto Co. on this. The key issue to us is the acceptance of this ingredient and that detergents with it are safe. Once that is there, our first priority is where the need for it is the greatest. That would be in the areas where phosphates are currently banned by law. That is where it is perfectly clear to us that those products will provide their greatest benefit.

My answer to your question really is, if this material is determined safe and we feel that there would be broad acceptance of that, we will go out and get some experience with it in a test market in one of these areas with bans. I would expect fully that we would be using the product in those kinds of areas broadly, in that 20 percent of the United States.

Mr. MAGUIRE. You would do that initially. Would you expect that you would then expand to the other 80 percent?

Mr. PEPPER. That is less certain. It would be quite dependent upon the relative costs as they develop over time of phosphate and NTA. You need to understand that today—and I think this point has been made—phosphate is a more cost-effective builder than NTA. NTA is the second best but it is still somewhat behind phosphate.

We can foresee the possibility that the combination at some level of phosphate and NTA would provide some additional benefit, but it is not of the same magnitude as we are seeing in the areas where phosphate is not used. We would be getting experience with it. We would do formulation work. We would hope that would lead to an improved product for consumers. We would have to see. Seeing would involve getting test experience with it.

Mr. MAGUIRE. We discussed the issue of people using material for handwashing of clothes or dishes earlier. I have heard what you had to say about the exchange with EPA on this subject.

Do you plan to warn consumers that use of laundry detergent with their hands in the dishpan or with clothes that are being washed by hands—

Mr. PEPPER. We would not think of marketing a detergent, Mr. Maguire, if we thought that dipping your hands into it to do the dishes, to clean up a floor, or to do some hand laundry was going to represent a risk. In the clarification to the EPA's letter that we received—

Mr. MAGUIRE. But they said it should not be used in hand dishwashing formulations.

Mr. PEPPER. No. Their clarification, Mr. Maguire, indicated—

Mr. MAGUIRE. Let me finish. If you extend that to a concern about whether people might, in fact, use a machine laundry detergent in the dishpan for clothes or for dishes, does not the same type of issue arise?

Mr. PEPPER. The second letter, the letter of clarification they sent to us, stated if you will read it—do you have it there? The EPA can speak about this in a moment better than I can, but it makes it perfectly clear. That their risk assessment on laundry detergents covered the normal uses of those detergents, including for hand laundry and for dishes. There is good reason that it did, because the material that has been submitted covers dermal exposure.

Mr. Winters, could you talk to that?

Mr. WINTERS. Yes. The information that was submitted in the EPA assessment that they went through took all the different routes of exposure and added them all up, including the hand dishwashing, including the quantity that comes from eating off of various utensils, all the way up and down the line. That is the kind of number they came up with. That was a clarification that they made back to us. It had taken all those into account. It just had not looked into these other areas. The dermal is the very, very low number because the transport through the skin is very, very low.

I would like to add one more point that may be a point of clarification.

I think the report to which you were referring to before that we inputted on was a Midwest Research Institute report covering only exposures of NTA. It should be made clear that the MRI report was not a risk assessment document. They came to us and asked us for data, as well as going to the other industries that would be involved and got data from those industries. Once that was written, it was sent to us for our critique. We found some various errors. That is the letter you are talking about that Mr. Hopping sent back.

Mr. MAGUIRE. Thank you. That is helpful, although the EPA does, of course, point out that the risk becomes greater. Instead of 1 in 500,000, it is 1 in 4,000 for dermal exposure, which applies I believe to workers.

Mr. WINTERS. That is incorrect, I believe. That has nothing to do with dermal exposure. The number that they are talking about, the high number is in the manufacturing of NTA if there is no protective equipment involved. That is what is entailed. It is assumed that all that is taken in is absorbed. That is a massive exaggeration.

Mr. MAGUIRE. When somebody uses this with their hands, presumably somewhere between what a worker would be exposed to and what somebody who just used it as a laundry detergent would be exposed to—

Mr. WINTERS. Someone who uses it with their hands is probably on the other side of the most conservative estimate because it just does not go through the skin to any appreciable extent. That will even be still lower than what you would get out of drinking water.

Mr. MAGUIRE. But you can breathe it if you are using it, too.

Mr. WINTERS. All those kinds of calculations are in the Midwest Research Institute report. That is a relatively insignificant

number, the inhalation from the process of doing the laundry in the laundry room.

Mr. MAGUIRE. Mr. Pepper, one of few major areas of significant railroad rate increases recently has been in the area of the shipment of phosphate rock. Are you aware of that? Has that had any impact on your numbers with respect to the cost of producing alternative types of detergent?

Mr. PEPPER. I am not familiar with the rail rates. I know that Monsanto might be able to talk to this better. We have seen increases and have been for quite a while in our phosphate costs. However, as I said to you before, the phosphate, even with these steep increases, is the most cost-effective builder that we have. NTA is pretty close. Then we fall back pretty far in terms of performance. It has not really changed the picture that I described before, Mr. Maguire.

Mr. MAGUIRE. Are there any other questions?

We thank you very much for your testimony today.

I think perhaps it is time for a short break.

[Brief recess.]

Mr. MAGUIRE. The subcommittee will come to order.

The next witness is Steven Jellinek, Assistant Administrator for Pesticides and Toxic Substances, U.S. Environmental Protection Agency.

Do you swear to tell the truth, the whole truth, and nothing but the truth, so help you God?

Mr. JELLINEK. I do.

Mr. MAGUIRE. Mr. Jellinek, you have a statement which we have read. I will leave it to you whether you want to read it in its entirety, whether you would like to summarize it, or whether you would like to move directly to questions. In any case, we will put it in the record in its entirety [see p. 155].

What do you prefer?

TESTIMONY OF STEVEN D. JELLINEK, ASSISTANT ADMINISTRATOR FOR PESTICIDES AND TOXIC SUBSTANCES, ENVIRONMENTAL PROTECTION AGENCY

Mr. JELLINEK. Thank you, Mr. Maguire. I would like to read certain parts of it for emphasis.

Mr. MAGUIRE. Fine. Proceed as you see fit.

Mr. JELLINEK. I will dispense with the background section. I think we have had enough in the way of that, and I do not have much to add. However, I would like to talk about how we got involved in this decision and why, and just for purpose of emphasis what we decided.

In about 1978, at around the same time that the IJC task force completed its review of the environmental effects of NTA, the Procter & Gamble Co. informed EPA that they were interested in resuming use of NTA as a substitute for phosphates in their laundry detergents sold in some areas of the United States. They asked EPA's Office of Pesticides and Toxic Substances, which I head, to assess the present state of knowledge concerning the possible health and environmental effects of NTA.

They believed that, as we have heard today, after many years of study and review, the weight of the evidence demonstrated the

safety of NTA, and they were willing to hold off making any final decision on reintroducing NTA until we completed our risk assessment.

Although we normally do not initiate risk assessments at the behest of industry, I thought that in this case Procter & Gamble's request was reasonable because of a number of unique factors.

First, the Federal Government, including EPA, had played an instrumental role in persuading the industry to withdraw NTA from the market in 1971.

Second, a large amount of scientific information on NTA was now available that was not available in 1971 and that had not been comprehensively reviewed by any Federal agency.

Third, in the intervening years a number of major foreign governments had permitted the use of NTA.

And, fourth, given the reported carcinogenicity of NTA and the potential for widespread exposure, we wanted to be in the best possible position to prevent resumption of its use if our review of the data led us to that conclusion.

Since NTA had been extensively tested and since the test results had been evaluated by expert committees, we decided that a relatively modest risk assessment effort would be the most logical way to proceed initially. We began our review in mid-1978, and, working at it when other projects permitted, completed it in April of this year.

Although our review was not conducted under the formal authority of a TSCA significant new use rule, it was, in effect, the functional equivalent of such an exercise. The main difference is that under the formal statutory scheme we would have had only 90 days to complete our review rather than the nearly 2 years we took to conduct a thorough evaluation. NTA has not been used in detergents sold in the United States during this 2-year period, and to the best of my knowledge the company still has made no final decision to use NTA.

Reviewing what we found, our risk assessment took a very conservative worst-case approach. At no point in our evaluation of NTA did we give the chemical the benefit of the doubt.

We assumed the 1 billion pounds of NTA would be marketed within just 2 years, by 1982, and that all U.S. laundry detergents marketed in every State would average 25 percent NTA. In contrast, if NTA is reintroduced mainly in phosphate ban areas, annual production would amount to about 250 million pounds. Furthermore, in Canada the industrywide average NTA content in laundry detergents is 15 percent by weight. Applying that percentage to U.S. use would lower production even further.

Our drinking water exposure estimates were based on the most recent Canadian monitoring efforts that used an analytical method sensitive to less than 0.2 parts per billion. Although these Canadian monitoring data show concentrations ranging from the level of detection to 24.5 parts per billion—and I might add they were taken during the colder winter months when NTA is less likely to degrade as rapidly as it degrades in the warmer waters—our risk assessment assumed that all concentrations would be at the highest level. That means we based our calculations on a scenario calling for every man, woman, and child in the United States to

drink 2 liters of water per day containing 24.5 parts per billion of NTA over a 75-year lifetime. We also assumed that each person would do one load of wash per day with an NTA detergent, and would wear only clothes washed in NTA over the same 75-year period.

Finally, in extrapolating from the experimental results in rats to predict those that could be manifested in the human population, we chose from among a number of statistical models the most conservative of those generally accepted by biostatisticians: the so-called one-hit model.

Furthermore, we did not adjust the model to take into account the likelihood that rats absorb NTA at anywhere from two to five times the rate humans do.

On the basis of these and other conservative assumptions, our risk assessment resulted in the following conclusions:

NTA is rapidly degraded under aerobic conditions at temperatures above 5° C.; the biodegradation of NTA does not lead to the formation of persistent intermediates. NTA can be decomposed in sunlit waters by photolysis, and the products of this decomposition are rapidly biodegradable.

NTA does not appear to solubilize metals from soils or to facilitate metal transport. In fact, the evidence suggests NTA increases adsorption of heavy metals by soils. Questions remain relating to the degradation of NTA in anaerobic and saline environments, as well as its behavior at extremes of environmental pH and its relationship to metals in sewage sludge and sediments.

Long-term and extensive Canadian monitoring data show that very low concentrations of NTA are found in drinking water. Similar levels are expected in this country. Estimated consumer exposure, too, is low, amounting to daily exposure of less than 1 microgram per kilogram for most adults. Worker exposure, though typically low, can be significant without protective equipment.

Oral, inhalation, and dermal absorption of NTA is relatively poor in humans, biotransformation is not measurable, and excretion is rapid. Because of its low acute and subchronic toxicity, NTA or its metabolites are not a high risk for these effects at expected exposure levels. NTA is not mutagenic and even in the presence of heavy metals does not cause teratogenic or reproductive effects. NTA has been shown to produce tumors in the kidneys and urinary tracts of both rats and mice exposed to very high dietary levels.

A conservative quantitative risk assessment estimates the oncogenic risk for the general population exposed through drinking water at 2 in 1 million. This risk estimate is consistent with one conducted earlier this year by the national toxicology program, as Dr. Rall discussed.

At the same time, the national toxicology program rejected the industry's conclusion that NTA is a threshold carcinogen. Exposure and oncogenic risks for detergent formulators are much higher than for the general population, although ways to greatly reduce exposure in an occupational setting are available.

Numerous studies on the acute and chronic effects of NTA on aquatic animals have generally demonstrated a low toxicity. Algal growth studies are conflicting, but NTA is not expected to signifi-

cantly increase nitrogen loadings to surface waters or contribute to eutrophication problems.

No obvious environmental problems have surfaced during the use of NTA in Canada over the last decade. At the low expected environmental concentrations, similar to those in Canada, no adverse environmental effects are anticipated, but confirmatory monitoring or testing under realistic conditions is needed.

Faced with the information contained in the EPA risk assessment of NTA, EPA concluded that the projected levels of exposure from the use of NTA in laundry detergents are generally low and therefore that the associated risks—including that of cancer—would also be low.

Based on these findings and on higher priority demands from EPA's limited resources, EPA further concluded that it would not pursue regulatory action against the resumed production and use of NTA for laundry detergents at this time. These conclusions are supported both by the Administrator of EPA and by the Agency's Office of Water and Waste Management.

I communicated these conclusions to Procter & Gamble in my letter of May 27, which included a full copy of the EPA risk assessment. I might add here that this was the first time that Procter & Gamble saw that risk assessment. The report that they commented on in draft was a contractor report on exposure based, in part, on data that we obtained from Procter & Gamble. We thought that since they were the main source of the data on consumer exposure, that it would be reasonable for them to see a draft of the contractor's report using their data.

My letter also contained a number of specific recommendations for companies manufacturing and processing NTA to follow to further reduce the likelihood that any harm might come from the use of this substance. Specifically, I recommended that:

Manufacturers and processors should employ strict controls to limit occupational exposures to NTA;

NTA should not be used in shampoos, foods, hand dishwashing detergents, and other consumer products designed to have direct dermal or oral exposures;

Manufacturers should conduct monitoring and environmental studies to confirm the predictions of low environmental levels during the initial years of resumed use, with EPA to participate in the design of such studies; and

Manufacturers and processors should maintain records of reported ingestions involving NTA-containing detergents.

We expect to receive periodic reports on Procter & Gamble's progress in observing our recommendations for monitoring and environmental studies.

Before closing, Mr. Chairman, I would like to make one final point. Although EPA has decided not to pursue regulation of NTA for the present, this neither constitutes an endorsement of NTA's use nor does it prevent us from taking regulatory action at any time in the future if additional data persuades us that NTA causes unreasonable risks to human health and the environment.

This concludes my prepared testimony. I shall be glad to answer any questions.

[Testimony resumes on p. 165].

[Mr. Jellinek's prepared statement follows:]

STATEMENT OF
HONORABLE STEVEN D. JELLINEK
ASSISTANT ADMINISTRATOR FOR
PESTICIDES AND TOXIC SUBSTANCES
U. S. ENVIRONMENTAL PROTECTION AGENCY
BEFORE THE
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS
COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE
U.S. HOUSE OF REPRESENTATIVES
June 26, 1980

Good morning, Mr. Chairman, and Members of the Subcommittee:

I have been asked to appear before you today to review EPA's recent actions with respect to nitrilotriacetic acid, or NTA. In particular, the Subcommittee has expressed an interest in my letter of May 27, 1980, notifying the Procter & Gamble Company of the results of EPA's risk assessment of the use of NTA in laundry detergents. I shall be pleased to discuss this letter and the circumstances surrounding EPA's evaluation of NTA.

Background

As Members of this Subcommittee know, NTA became important to the detergent industry in the late 1960s as a replacement for phosphates in laundry products. Detergent phosphates had come under scrutiny as the principal and most controllable cause of eutrophication in lakes. Anticipating public and legislative pressure to reduce the phosphorous content of detergents, detergent manufacturers and suppliers geared up for the large-scale production of NTA.

In late 1970, preliminary findings from a study conducted at the National Institute of Environmental Health Sciences (NIEHS) suggested that NTA might increase the teratogenic activity of methylmercury. Based on these preliminary findings, the major detergent manufacturers and suppliers agreed, at the request of the Surgeon General and the EPA Administrator, to discontinue the use of NTA, pending further study.

Although the concerns raised in the original NIEHS study were refuted after subsequent review and testing by the U.S. Department of Health, Education and Welfare (HEW), and by the industry, other concerns arose regarding NTA. In 1974, HEW found that an NIEHS study of NTA in the drinking water of rats indicated that the substance had a carcinogenic effect on the rodents' urinary tract. A later bioassay conducted at the National Cancer Institute (NCI) confirmed these results.

A number of evaluations of NTA have been performed since the NCI bioassay. For example, because interest in banning phosphates from detergents persisted throughout the 1970s, the International Joint Commission (IJC)--a U.S./Canadian advisory group on the quality of Great Lakes water--formed two task forces to take a closer look at the health and environmental implications of NTA. In 1977, the IJC's health task force concluded that NTA

is neither a mutagen nor a teratogen, and that it had a low probability of causing cancer in humans. In 1978, the IJC's environmental task force concluded that there is nothing in the scientific literature or from Canadian experience to indicate that NTA presents an environmental hazard, but recommended that additional studies accompany any resumption of its use in this country.

The annual production of NTA in the United States is currently 70-75 million pounds. At the present time, most of this (60-65 million pounds) is exported for use in detergents. NTA has been used in Canada since the early 1970s; it is also used in Finland, Sweden, the Netherlands, and Norway. The remaining 10-15 million pounds of U.S. production is used domestically in a variety of applications. NTA is currently produced in the United States by only two companies, Monsanto and W. R. Grace.

The most promising market for NTA use in the United States is in areas where phosphorus is currently banned or limited, which constitute 20-25 percent of the total detergent market. In addition, other areas might initiate action to ban or limit phosphates if NTA becomes available.

How EPA Got Involved and Why

In 1978, at about the same time that the IJC task force completed its review of the environmental effects of NTA,

the Procter & Gamble Company informed EPA that they were interested in resuming use of NTA as a substitute for phosphates in their laundry detergents sold in some areas of the United States. They asked EPA's Office of Pesticides and Toxic Substances, which I head, to assess the present state of knowledge concerning the possible health and environmental effects of NTA. They believed that, after many years of study and review, the weight of the evidence demonstrated the safety of NTA and they were willing to hold off making any final decision on reintroducing NTA until we completed our risk assessment. Although we normally do not initiate risk assessments at the behest of industry, I thought that, in this case, Procter & Gamble's request was reasonable because of a number of unique factors. First, the Federal Government--including EPA--had played an instrumental role in persuading the industry to withdraw NTA from the market in 1971. Second, a large amount of scientific information on NTA was now available that was not available in 1971 and that had not been comprehensively reviewed by any Federal agency. Third, in the intervening years a number of major foreign governments had permitted the use of NTA. And fourth, given the reported carcinogenicity of NTA and the potential for widespread exposure, we wanted to be in the best possible position to prevent resumption of its use if our review of the data led us to that conclusion.

Since NTA had been extensively tested and since the test results had been evaluated by expert committees, we decided that a relatively modest risk assessment effort would be the most logical way to proceed initially. We began our review in mid-1978, and, working at it when other projects permitted, completed it in April of this year.

Although our review was not conducted under the formal authority of a TSCA significant new use rule, it was, in effect, the functional equivalent of such an exercise. The main difference is that under the formal statutory scheme, we would have had only 90 days to complete our review rather than the nearly 2 years we took to conduct a thorough evaluation. NTA has not been used in detergents sold in the United States during this 2-year period, and to the best of my knowledge the company still has made no final decision to use NTA.

What We Found

Our risk assessment took a very conservative worst-case approach. At no point in our evaluation of NTA did we give the chemical the benefit of the doubt.

We assumed that one billion pounds of NTA would be marketed within just 2 years (by 1982), and that all U.S. laundry detergents marketed in every state would average 25 percent NTA. In contrast, if NTA is reintroduced mainly

in phosphate ban areas, annual production would amount to about 250 million pounds. Furthermore, in Canada the industry-wide average WTA content in laundry detergents is 15 percent by weight. Applying that percentage to U.S. use would lower production even further.

Our drinking water exposure estimates were based on the most recent Canadian monitoring efforts that used an analytical method sensitive to less than 0.2 parts per billion (ppb). Although these Canadian monitoring data show concentrations ranging from the level of detection to 24.5 ppb, with a national mean of 2.82 ppb, our risk assessment assumed that all concentrations would be at the highest level. That means we based our calculations on a scenario calling for every man, woman, and child in the United States to drink two liters of water per day containing 24.5 ppb of WTA over a 75-year lifetime. We also assumed that each person would do one load of wash per day with an WTA detergent, and would wear only clothes washed in WTA over the same 75-year period. Finally, in extrapolating from the experimental results in rats to predict those that could be manifested in the human population, we chose from among a number of statistical models the most conservative of those generally accepted by bio-statisticians: the "one-hit" model.

Furthermore, we did not adjust the model to take into account the likelihood that rats absorb NTA at anywhere from two to five times the rate humans do.

On the basis of these and other conservative assumptions, our risk assessment resulted in the following conclusions:

NTA is rapidly degraded under aerobic conditions at temperatures above 5°C; the biodegradation of NTA does not lead to the formation of persistent intermediates. NTA can be decomposed in sunlit waters by photolysis, and the products of this decomposition are rapidly biodegradable. NTA does not appear to solubilize metals from soils or to facilitate metal transport. In fact, the evidence suggests NTA increases adsorption of heavy metals by soils. Questions remain relating to the degradation of NTA in anaerobic and saline environments, as well as its behavior at extremes of environmental pH and its relationship to metals in sewage sludge and sediments.

Long-term and extensive Canadian monitoring data show that very low concentrations of NTA are found in drinking water. Similar levels are expected in this country. Estimated consumer exposure, too, is low, amounting to daily exposure of less than 1 ug/kg for most adults. Worker exposure, though typically low, can be significant without protective equipment.

Oral, inhalation, and dermal absorption of NTA is relatively poor in humans, biotransformation is not measurable, and excretion is rapid. Because of its low acute and subchronic toxicity, NTA or its metabolites are not a high risk for these effects at expected exposure levels. NTA is not mutagenic and even in the presence of heavy metals does not cause teratogenic or reproductive effects. NTA has been shown to produce tumors in the kidneys and urinary tracts of both rats and mice exposed to very high dietary levels. A conservative quantitative risk assessment estimates the oncogenic risk for the general population exposed through drinking water at two in one million. This risk estimate is consistent with one conducted earlier this year by the National Toxicology Program (NTP), also at the request of Procter & Gamble; at the same time, the NTP rejected the industry's conclusion that NTA is a threshold carcinogen. Exposure and oncogenic risks for detergent formulators are much higher than for the general population, although ways to greatly reduce exposure in an occupational setting are available.

Numerous studies on the acute and chronic effects of NTA on aquatic animals have generally demonstrated a low toxicity. Algal growth studies are conflicting, but NTA is not expected to significantly increase nitrogen

loadings to surface waters or contribute to eutrophication problems. No obvious environmental problems have surfaced during the use of NTA in Canada over the last decade. At the low expected environmental concentrations (similar to those in Canada), no adverse environmental effects are anticipated, but confirmatory monitoring or testing under realistic conditions is needed.

Faced with the information contained in the EPA risk assessment of NTA, EPA concluded that the projected levels of exposure from the use of NTA in laundry detergents are generally low and therefore that the associated risks--including that of cancer--would also be low. Based on these findings and on higher priority demands for EPA's limited resources, EPA further concluded that it would not pursue regulatory action against the resumed production and use of NTA for laundry detergents at this time. These conclusions are supported both by the Administrator of EPA and by the Agency's Office of Water and Waste Management.

I communicated these conclusions to Procter & Gamble in my letter of May 27, which included a full copy of the EPA risk assessment. My letter also contained a number of specific recommendations for companies manufacturing

and processing NTA to follow to further reduce the likelihood that any harm might come from the use of this substance. Specifically, I recommended that:

- manufacturers and processors should employ strict controls to limit occupational exposures to NTA;
- NTA should not be used in shampoos, foods, hand dishwashing detergents, and other consumer products designed to have direct dermal or oral exposures;
- manufacturers should conduct monitoring and environmental studies to confirm the predictions of low environmental levels during the initial years of resumed use, with EPA to participate in the design of such studies;
- and that manufacturers and processors should maintain records of reported ingestions involving NTA-containing detergents.

We expect to receive periodic reports on Procter & Gamble's progress in observing our recommendations for monitoring and environmental studies.

Before closing, Mr. Chairman, I would like to make one final point very clear today: Although EPA has decided not to pursue regulation of NTA for the present, this neither constitutes an "endorsement" of NTA's use nor does it prevent us from taking regulatory action at any time in the future if additional data persuades us that NTA causes unreasonable risks to human health and the environment.

This concludes my prepared testimony, Mr. Chairman.

I shall be glad to answer any questions.

Mr. MAGUIRE. Mr. Jellinek, what would you say are the societal benefits that justify the introduction of a known carcinogen into the environment?

Mr. JELLINEK. Mr. Maguire, as I said in my testimony, we only reviewed the risk of NTA. We conducted a preliminary risk assessment of NTA primarily designed to decide whether or not we should regulate it. We did not do any detailed review of the benefits of NTA as we would if we had decided to take regulatory action.

Mr. MAGUIRE. You did not review the benefits of this decision. Therefore, there was no risk-benefit judgment made?

Mr. JELLINEK. There was not a risk-benefit judgment made. We decided in essence that because of the low risks, because of our limited resources, it was not a high priority for us to devote additional resources to, given the many other responsibilities we have under TSCA.

Mr. MAGUIRE. According to the notes of the March 11, 1980, meeting which you had with Procter & Gamble and Monsanto representatives—and these notes were done by Justine Welch of your staff—you told Procter & Gamble "we were not in the business of endorsing chemicals, particularly known carcinogens."

Mr. JELLINEK. That is correct. We told Procter & Gamble that.

Mr. MAGUIRE. How does that square with the letter that you sent them on May 27, 1980?

Mr. JELLINEK. The simple answer is that our letter of May 27 does not constitute an endorsement of NTA.

Mr. MAGUIRE. Aren't we splitting hairs a little bit here? If, in fact, the letter that you sent on May 27, 1980, has the practical effect of permitting, if not indeed encouraging, the introduction of a cancer-causing substance into the marketplace and into the ground water, a substance which had not previously been used as a detergent builder over a 10-year period because of previous requests by responsible Government officials that it not be used, how can you characterize your decision of May 27 in the way that you have as not an endorsement, not a regulatory decision? The fact is

that you did an enormous amount of work on this, as you yourself indicate, over a couple years. You produced a letter which Procter & Gamble indicated to us today was what they felt they had to have before they could move ahead to market the product with this formulation.

Aren't we splitting hairs here when you characterize this as a nonendorsement and a nonregulatory decision?

Mr. JELLINEK. No; I do not think we are. First of all, we had no knowledge that Procter & Gamble would not go ahead regardless of what the results of our risk assessment were. We did a straightforward, scientific review of the data and gave a straightforward answer based on what that data told us. On the basis of that answer we concluded and reported honestly that it was not a high priority for the use of our resources to further regulate NTA.

Mr. MAGUIRE. You have described in your statement that the process you undertook was the functional equivalent of a process under the significant new use provisions of the law. If that is the case, how can you continue to characterize the results of that functional equivalent as a nonregulatory decision or a nonendorsement when in fact you have told people to go ahead and use it?

Mr. JELLINEK. The significant new use provisions of the law in the first instance simply state that if EPA determines that a new use of a chemical is significant, the manufacturer has to notify EPA 90 days before beginning the manufacture of that new chemical. If we had a formal significant new use rule in effect on NTA, then 90 days before Procter & Gamble or Monsanto intended to manufacture for this use they would have to notify us. We would then have 90 days to review whatever data was available and decide whether or not to stop the chemical at that point or to let it go on.

In this case we had a situation where the company voluntarily informed us of its intent to use this chemical in a "new use," for purposes of our discussion, and was willing to wait voluntarily as long as it took for us to complete our risk assessment. I might say we did not work on it every day out of the 2 years. As I said, it was a relatively modest effort. We spent approximately three-quarters of a person year effort on it and about \$30,000 in contract funds.

Mr. MAGUIRE. Mr. Rinaldo, did you wish me to yield?

Mr. RINALDO. Yes. I am sorry I was not here earlier to listen to all of your testimony. I am particularly interested in this inasmuch as I serve as the ranking minority member on the Consumer Protection and Finance Subcommittee which specifically oversees EPA's implementation of the Toxic Substances Control Act.

As you know, when TSCA was first drafted we recognized that EPA would be called upon to make some very difficult scientific decisions. I also recognize that a risk-free environment is not possible. Therefore, what we need is a risk assessment approach which is logical and which should be encouraged.

I want to state that certainly I am not qualified and I am attempting to second-guess the scientific judgments made by the agency. However, the agency has been criticized—I have heard some criticism—over the fact that you have not used section 5, the significant new use authority.

Inasmuch as we got into that area, a discussion of section 5 and the significant new use authority, had you used section 5 in retrospect what would you have done differently?

Mr. JELLINEK. It is hard to answer that question with confidence. I assume if we had been able to do the same three-quarters of a year's analysis in a 90-day period we would have come out the same way, assuming all of that data were available to us through the significant new use process.

The significant new use rule gives us a chance to stop and take a look at a proposed new use of a chemical and to review whatever data is available. We would have presumably had the same data available and taken the same look and our scientists would have come up with the same risk assessment. But, they would have had to work 24 hours a day.

Mr. RINALDO. How do you account for the fact that one member of the scientific panel stated that, had section 5 been used, the fact that you were looking at NTA would have been noticed in the Federal Register and the scientific community would then be able to review the science on which you based your decision not to take regulatory action against NTA at this time?

Mr. JELLINEK. First of all, that is technically correct. The fact that we were reviewing NTA would have been in the Federal Register and members of the public who were interested in it could have brought their points of view to our attention as we conducted our review. Assuming that we came to the same conclusion, we would have written a proposed decision and made available our copy of the risk assessment.

In fact, NTA has been extensively studied in a very public forum for a number of years now. The International Joint Commission, in particular, has prepared reports that have been public and that have been commented on and available for the public to comment.

Frankly, I consider this hearing, at least in one aspect, a public review and comment on our risk assessment and our decision. Don't forget, our decision was a decision not to do something. It was not a decision to do something.

Our report is available. If new data becomes available to us, if through an open public comment process we learn something that we did not review in our risk assessment or that was not available in the years that NTA has been studied, then we still have the option to take regulatory action against it.

Mr. RINALDO. You are saying you would have done everything the same way.

Mr. JELLINEK. I am saying I assume the conclusion of our scientists would have been the same.

Mr. RINALDO. If you had done it the other way, the whole process would have been speeded up.

Mr. JELLINEK. That is true, but the fact is that the company came in and said, "We are not planning on manufacturing this thing. We are considering manufacturing it. We invite you to review the data that has accumulated over the intervening years before we make a decision." We would have had to do it faster; you are absolutely right.

Mr. RINALDO. You would have had to do it within 90 days.

Mr. JELLINEK. Within 90 days, as I said in my testimony.

Mr. RINALDO. Could you do as thorough a study in 90 days?

Mr. JELLINEK. I think by definition we would not have been able to do as thorough a study.

Mr. RINALDO. I am on my colleague's time. I just want to ask one final question.

Do you believe that the statute needs to be amended to clarify that risk assessment analysis as a legitimate regulatory tool?

Mr. JELLINEK. I do not think that is necessary. The statute as it stands makes the regulatory standard very clear and provides us with the ability to do risk assessments within that standard.

Mr. RINALDO. Thank you very much.

I want to thank my colleague for yielding.

Mr. MAGUIRE. I appreciate the gentleman's participation.

Mr. Jellinek, on June 9 Mr. Beck, Assistant Administrator for Water and Waste Management, told the Subcommittee on Health and the Environment that EPA has an agency steering committee. The steering committee requires that any regulatory action that goes forward ultimately needs the concurrences of each of the Assistant Administrators. Yet, he indicated—and documents provided by your office to the subcommittee indicate—concurrences of each of the Assistant Administrators concerning your letter of May 27 to Procter & Gamble were not obtained in advance of the issuance of your letter.

Can you tell us why that was the case?

Mr. JELLINEK. Yes. At the risk of getting involved in hair splitting and semantics again, the fact is that our decision of May 27 was not a regulation. Therefore, it did not go through this steering committee process.

Mr. MAGUIRE. This is marvelous. If somebody with an interest can come in from the outside and get you to make a decision which you do not describe as a regulatory decision, the decision is then immune from any of the provisions of law or provisions of administrative procedure.

Mr. JELLINEK. Mr. Maguire, as I said, there existed unique circumstances under which we decided to get into this. As a health and safety regulator with literally tens of thousands of potential targets for regulation, and whether we like it or not, we make decisions very often not to do things because we cannot do everything.

Mr. MAGUIRE. My contention is that you did something here.

Mr. JELLINEK. That's right, we did.

Mr. MAGUIRE. Let me ask you this: You said that this is the functional equivalent of an examination of a significant new use. I am suggesting to you—and I would like your comment on this—that if that was the functional equivalent of such an examination, then the results of it are the functional equivalent of a regulatory decision.

Mr. JELLINEK. In a sense, that is correct.

Mr. MAGUIRE. This is not a regulatory decision but it is the functional equivalent of a regulatory decision.

Mr. JELLINEK. That is an accurate description.

Mr. MAGUIRE. Is it not then important that the functional equivalent of consultations under the established procedures and under

the law take place if in fact the decision is the functional equivalent? Don't we need the functional equivalent of a process as well?

Mr. JELLINEK. Our proposed decision on this was referred to the Office of Drinking Water before any decision went out of the agency. It was referred to the Office of the Administrator. We did not go through the formal steering committee review process.

Mr. MAGUIRE. It looks to me from examining the record as if certain very important actors were not consulted at all—for example, the Surgeon General of the United States. It also looks to me as if the people that you did "consult" were not given the opportunity to review the evidence and comment on the decision.

For example, the note of your unit to Victor Kim, Deputy Assistant Administrator for Drinking Water, says that "because the resumed use of this low level carcinogen will likely result in detectable quantities appearing in drinking water, I wanted you to be aware of our office's assessment of the hazards," et cetera.

Then you go on to formulate this highly questionable bit of legerdemain that you recommend allowing but not endorsing the resumed use of NTA. Then you go on to say, "If you would like to discuss our assessment or our report, please call me." Did they call you?

Mr. JELLINEK. No.

Mr. MAGUIRE. Did you call them?

Mr. JELLINEK. No.

Mr. MAGUIRE. Therefore, once this piece of paper was sent, that was it?

Mr. JELLINEK. They had an opportunity to call us. Let me take it back. I can find out for you whether or not my staff called to follow up as to whether they had had a chance to look at this.

Mr. MAGUIRE. You have submitted a list here in answer to the subcommittee's questions of the various consultative contacts that took place. There is no notation there that anybody followed up with the Drinking Water Office.

Mr. JELLINEK. I cannot be sure. I can check that out for you.

Mr. MAGUIRE. In case you find something that indicates that you did, we will leave the record open.

Mr. JELLINEK. I can assure you, because this did come up at a hearing with Mr. Beck, as you noted, we have talked with them since then in some detail. They do support the decision.

Mr. MAGUIRE. It is interesting that we had asked him for his response on the record. We have not yet received that.

Mr. JELLINEK. I think it is in preparation.

Mr. MAGUIRE. You wrote a memo to the Administrator on May 8, 1980, in which you indicated that, if he wished, a briefing would be arranged. Was such a briefing arranged?

Mr. JELLINEK. No.

Mr. MAGUIRE. Did you hear back from him that he desired not to have a briefing?

Mr. JELLINEK. We did consult with his staff, and that was the result of that.

Mr. MAGUIRE. The decision is he did not want to have a briefing?

Mr. JELLINEK. He did not want a briefing; that is right.

Mr. MAGUIRE. Was that one that he made or that his staff made?

Mr. JELLINEK. I honestly do not know. I can find that out for you.

Mr. MAGUIRE. We will leave the record open for any further information on that point.

[The following statement was received for the record:]

This decision was made by the Administrator, himself.

Mr. JELLINEK. I assume he made it. I assume he made the decision.

Mr. RINALDO. Excuse me. Mr. Chairman, is that memo you are reading from going to be submitted for the record? I do not believe we have received a copy of the responses on this.

Mr. MAGUIRE. The gentleman will be provided with those documents.

That particular document should be placed in the record, the memorandum of May 8 from Mr. Jellinek to the Administrator. [The memorandum referred to follows:]

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MAY 8 1980

OFFICE OF TOXIC SUBSTANCES

SUBJECT: NTA Detergent Builders

FROM: Steven D. Jellinek
Assistant Administrator
for Pesticides and Toxic Substances (75-788)

TO: The Administrator

Resumed Use of NTA in Detergents

The Proctor and Gamble Corporation plans to resume use in its household laundry detergents of a substance which is a low level carcinogen. The substance, nitrilotriacetic acid (NTA), would be used in the relatively few areas where phosphates are now banned. However, if it were used more broadly over the U.S., production volume could reach 1 billion pounds per year. I am providing this memorandum to inform you of my recommendation that EPA not object to Proctor and Gamble's action and to arrange to brief you on this matter if you so desire.

Background

NTA became important in the detergent industry in the late 1960's when detergent phosphates were determined to be the principal cause of eutrophication problems in lakes. Anticipating public and legislative pressure to reduce the phosphorous content of detergents, manufacturers geared up for the large scale production of NTA as an alternative to phosphates.

In 1970, preliminary findings from a study conducted at the National Institute of Environmental Health Sciences (NIH) suggested that NTA might increase the teratogenic activity of methylmercury. Based on these preliminary findings and at the request of the Surgeon General, the major detergent manufacturers and suppliers agreed to voluntarily discontinue the use of NTA in the U.S.

Although the concerns raised by this study were refuted by subsequent review and testing efforts by the industry and DHEW, new concerns were raised regarding the carcinogenic potential of NTA. In 1974, an NTA subcommittee was formed in DHEW to evaluate an NIEHS study of NTA in the drinking water of rats. The subcommittee found that the study indicated NTA had a carcinogenic effect on the urinary tract of the rats in the test. Later, an MCI bioassay confirmed these results. Because the movement to ban phosphates from detergents persisted, the International Joint Commission (IJC)* formed a task force to take a close look at the health implications of NTA. In 1977, the task force issued a report which concluded:

- o The available data do not indicate that NTA is a teratogen or a mutagen;
- o The only evidence that might cause concerns regarding the health of workers and the general population is the NIEHS study which showed cancer of the urinary tract in rats and mice given large doses of NTA over their lifetime.
- o At levels of NTA to which humans are exposed, the highest probability of tumor formation in rodents is within an order of magnitude of 1 in 2 million.

The International Joint Commission also formed a task force on the environmental effects of NTA which completed its findings in 1978. The task force concluded that there is nothing in the literature or from the Canadian experience to indicate that the use of NTA would present an environmental hazard. However, because of concern over certain gaps in knowledge of the environmental effects of NTA, the task force recommended that studies be conducted to address specific questions if the use of NTA is resumed in this country.

Production, Uses and Exposure

Currently, Monsanto and W.R. Grace are the only U.S. companies producing NTA. The annual production is 70-75 million pounds; 60-65 million pounds of this is exported to Canada and Europe where it is used as a detergent builder. The

* A joint Canadian-U.S. advisory group concerned with the water quality of the Great Lakes.

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remaining 10-15 million pounds are used domestically in a variety of applications (industrial water treatment, metal cleaning, institutional cleaners and textile preparation).

Proctor and Gamble currently plans to introduce use of NTA into areas that now ban phosphate detergents (i.e., most States bordering on the Great Lakes; New York, Michigan, Indiana, Minnesota, Wisconsin and others). Use in these areas may result in production volumes of 209-277 million lbs per year. If NTA were used nationwide, production could reach 1 billion pounds per year. Almost all of that would be released to the environment.

Small numbers of people (less than 3,000 total) would be exposed to NTA during its manufacture and formulation. We estimate the potentially exposed population for the initial phosphate replacement areas to be approximately 50 million people. If NTA replaces phosphate across the board, virtually the entire U.S. population has the potential for continuous low level exposure in drinking water and consumer detergent products. Long term and extensive Canadian monitoring data show that very low concentrations of NTA are found in drinking water (national mean = 2.82 ug/l; range from 0.2 to 24.5 ug/l); similar levels are expected in the U.S. Worker exposure, though typically low, can be significant for the few working without protective equipment in the dustiest part of the operation.

Recommendation

At the request of Proctor and Gamble and Monsanto, I have had the Office of Testing and Evaluation conduct a preliminary assessment of the health and environmental risks that may be presented by the use of NTA. That assessment indicates the risks associated with the use of NTA to be low. Although I do not recommend that the Agency endorse the resumed use of NTA, I believe we should be prepared to publicly state, if asked, that we have independently reviewed the issue and found that generally the risks associated with the use of NTA are low. Therefore, because there are no regulatory constraints prohibiting the production or use of NTA, EPA will not act to prevent the domestic use of NTA in household detergents. We will, however, recommend that manufacturers conduct specific monitoring and environmental studies during the initial years of resumed use. We will also recommend that workers wear protective equipment in the dustiest part of the production process and notify OSHA of our recommendation to allow them to take any appropriate action.

Because of the imminence of Proctor and Gamble's production plans, we may have to give our position on this issue before the middle of May. Therefore, if you do not request a briefing on this issue before May 15, I will assume you agree with my recommendation.

Mr. MAGUIRE. The memorandum concludes with this statement: "Because of the imminence of Procter & Gamble's production plans, we may have to give our position on this issue before the middle of May."

First of all, does the imminence of their production plans determine when you do and do not have to make decisions?

Mr. JELLINEK. No, it does not.

Mr. MAGUIRE. Why did you say that in the letter?

Mr. JELLINEK. The assumption was that if P. & G. announced that they were going to begin to use NTA again, then we would have to have a public position on that because we would be asked what EPA's position was. We had finished the risk assessment.

Mr. MAGUIRE. It was pretty clear, having gone through such an elaborate consultation with you over such a long period of time, that they were surely not going to introduce it unilaterally.

Mr. JELLINEK. That is something that I could not assume.

Mr. MAGUIRE. That sentence, of course, has the unfortunate implication that you were working on their schedule rather than your own.

Mr. JELLINEK. You may read that, but I don't.

Mr. MAGUIRE. You don't read that?

Mr. JELLINEK. No.

Mr. MAGUIRE. The final sentence says, "Therefore, if you do not request a briefing on this issue before May 15, I will assume you agree with my recommendation." I take it you did not hear from the Administrator by May 15.

Mr. JELLINEK. That is correct.

Mr. MAGUIRE. Therefore, you assumed that he agreed with your recommendation?

Mr. JELLINEK. We heard from his staff.

Mr. MAGUIRE. What did you hear from the staff?

Mr. JELLINEK. We heard from his staff that he did agree with the recommendation.

Mr. MAGUIRE. That he did agree with the recommendation?

Mr. JELLINEK. That is correct.

Mr. MAGUIRE. I am afraid we are going to have to break to vote. We will resume as soon as possible, probably in about 12 or 15 minutes.

[Brief recess.]

Mr. MAGUIRE. Mr. Jellinek, we were talking about your statement that the review that you conducted was the functional equivalent of a review under the new use section of the TSCA law. I suggested that in that case the decision that you made at the end of the review probably ought to be understood to be a functional equivalent of a regulatory decision. You agreed that it was.

I then suggested that it seemed to me that, if that were the case, then there ought to be also a functional equivalent of the proper procedures followed in the course of the review, which would, of course, involve consultation and approvals by others in addition to yourself.

You took the position, if I understood it correctly, that none of this procedural matter was relevant because of the fact that it was not a regulatory decision and that the functional equivalent of a regulatory decision, which is what you felt this could be accurately

described to be, made you immune from the processes that are otherwise required under the administrative procedures that have been set up for dealing with cancer policy and from the law itself.

Is that a fair summary of the exchange we had just before the break?

Mr. JELLINEK. I think the conclusion is a little stronger than I would make it in terms of "immunity". In my program and in other EPA programs, and probably in other regulatory agencies, we very often have to make decisions not to do things, not to regulate, because we want to devote ourselves to regulating other things that we think are more important.

Normally in EPA and in other agencies, those decisions not to regulate are not subject to the same kind of reviews or administrative procedures as decisions to regulate are. That is the system that is developed both in the EPA and in agency practice.

Mr. MAGUIRE. Therefore, a regulatory decision in your judgment is only a decision which is, in fact, a decision to regulate; is that correct?

Mr. JELLINEK. That is shorthand. We make some regulatory decisions that are not decisions to regulate but are decisions to get information or decisions to request a review of some kind.

Mr. MAGUIRE. If P. & G. in its testimony can refer to the "tacit approval from EPA" for the marketing of detergents with NTA and in fact plan to move ahead only with the affirmative decision which you have made, however you wish to characterize it, then it has the impact, you have agreed, of a regulatory decision on your part in that the public will now be exposed, whatever the hazards may or may not be, up to a billion pounds or more of a known cancer-causing substance in the ground water supply. Is that not correct?

Mr. JELLINEK. If they go ahead, the public will be exposed to NTA at low levels.

Mr. MAGUIRE. Your estimates suggest up to or more than 1 billion pounds when the marketing is fully developed?

Mr. JELLINEK. For purposes of our risk assessment, we used those numbers to make our worst case. We do not know whether NTA will be produced in that amount. There are good reasons to believe that it will be less than that amount. Nevertheless, those are the numbers we used in order to be conservative and to do a conservative worst-case risk assessment.

Mr. MAGUIRE. Did it strike you that it might be appropriate to review this matter with the interagency group on cancer policy?

Mr. JELLINEK. I am not sure what you mean by the interagency group on cancer policy.

Mr. MAGUIRE. The IRLG.

Mr. JELLINEK. The Interagency Regulatory Liaison Group. First of all, let me give you some background.

The National Toxicology Program Executive Committee, which includes representatives from each of the IRLG agencies as well as representatives from their research agencies, was aware of our activity on NTA.

Mr. MAGUIRE. Everybody was aware of your activity. Your submission says "We discussed it with so and so. We made so and so aware that we were working on this." However, nobody, as near as

we have been able to determine, was aware of the decision or of the text of the letter itself prior to the issuance of the May 27 letter.

Mr. JELLINEK. None of the IRLG agencies were. Dr. Rall was.

Mr. MAGUIRE. The water people in your own agency were not aware of the May 27 decision.

Mr. JELLINEK. The drinking water people were.

Mr. MAGUIRE. They were not.

Mr. JELLINEK. They were.

Mr. MAGUIRE. Mr. Beck was not.

Mr. JELLINEK. Mr. Beck was not, but Mr. Kim and his staff were.

Mr. MAGUIRE. I am sensitive to the fact that the gentleman from Connecticut is back. Would you like me to yield to you?

Mr. MOFFETT. Yes; just for a moment, Mr. Chairman.

There is one thing I do not understand. What is this business about making a decision not to regulate? What was there forcing you to make a decision not to regulate?

Mr. JELLINEK. As I explained in my testimony, we decided to enter into this risk assessment because of the unique circumstances surrounding the decision to remove NTA from the market.

Mr. MOFFETT. I read the testimony and your reason for going into it. However, nowhere do I find what was binding you to come down with a decision not to regulate.

Mr. JELLINEK. At the end of the risk assessment we felt that it was reasonable to tell the industry whether or not we would regulate—based on what we found. They had said that they were considering using NTA. We thought informing them of our decision was a reasonably straightforward way to approach the results of our risk assessment.

Mr. MOFFETT. I still do not understand.

Mr. JELLINEK. We were not compelled to do it.

Mr. MOFFETT. Was it a courtesy to the industry? Is that what you are saying?

Mr. JELLINEK. It was not a courtesy to the industry. It was a response to their request.

Mr. MOFFETT. What you are telling me then is that the industry is in the position of deciding whether or not a decision to regulate is made.

Mr. JELLINEK. That is not true.

Mr. MOFFETT. I am all for giving industry clear signals and so forth, but what was there that was forcing you to come down with a decision at this time not to regulate or to regulate? What was there?

Mr. JELLINEK. There was nothing forcing us to do it. We thought it was a reasonable thing to do, having finished this risk assessment, which we conducted at their request because of the unique circumstances which led to the removal of the product from the market by Government without public participation, without Federal Register notice. There was no process back in 1970 when it was withdrawn.

Mr. MOFFETT. Does that make this process correct?

Mr. JELLINEK. No; there has been a lot of process since.

Mr. MOFFETT. Where has there been an opportunity for a public hearing on this and so forth since? On how many occasions?

Mr. JELLINEK. First of all, as I told Mr. Maguire, the results of the studies conducted over the years have been publicly available. The International Joint Commission has conducted two thorough and public reviews of it. EPA's decision is publicly available. This is in essence—

Mr. MOFFETT. No; that is not what I am saying. I have people back home who are involved with lakes associations and lake management. They are very active people. They like to go and testify at different things. What opportunity have they had to testify on NTA at a public hearing sponsored by the EPA or other agencies, for that matter?

Mr. JELLINEK. Our risk assessment is available.

Mr. MOFFETT. I know that. Come on now. Has there been an opportunity or hasn't there? Do we have this long trail of nonparticipation back for a decade on this issue? That is what I am trying to discover. I had not even thought of it that way but, since you raised the issue that there never was a full adjudicatory proceeding or a full agency proceeding, now it occurs to me that maybe we have had a decade of people like the people I have back home in lakes associations not having had the opportunity to testify in any kind of session. Is that true or is it not true?

Mr. JELLINEK. As far as I know, there has not been any EPA public hearing held on it. I am not sure about whether the Joint Commission has held public hearings or not. It may have.

Mr. MOFFETT. The Joint Commission is not a Government agency.

Mr. JELLINEK. No; they are quasi-government.

Mr. MOFFETT. I am talking about an agency that these people are paying for with their taxpayers' dollars.

This is what I do not understand. There is an implication in what you are saying here about, "Well, there are a lot of things we have to do and we have various responsibilities under the law. Some things are more dangerous than others. We only have limited resources. Therefore, we have to go after the things that are the most serious."

Fine. I do not disagree with that at all. I am just not sure how that fits in with this business of, "Well, we had to make a decision not to regulate." I do not see that. It is not clear to me how you get into the position where you have to make a decision not to regulate.

Let's suppose you did the risk assessment and you involved other agencies and so forth. As with some other things, as close as you could discern what the consensus was, it seemed to be we don't really know but we just cannot permit this to come back on the market.

Inasmuch as you have characterized this as making the decision not to regulate, what would that be in terms of a decision to regulate—in other words, saying we are not going to let it back on the market? What is entailed in your regulation from that point? What is the burden on you? What is the burden on the agency's resources?

Mr. JELLINEK. If we decided to regulate—

Mr. MOFFETT. No. If you decided under that scenario, which I am assuming you would call regulate, if you made a decision that you

were going to continue going with the status quo which has been in existence now for many years, under the way you have portrayed this thing that would be a decision to regulate; is that right? Wouldn't it?

Mr. JELLINEK. Yes.

Mr. MOFFETT. What is the burden? The implication of what you are saying is that you made this decision not to regulate because there are other things and you only have so much in the way of resources and so forth. I am trying to determine from you what burden would come down on you if you had not made this decision which was a decision not to regulate.

Mr. JELLINEK. It would really depend upon whether the industry went ahead and introduced the chemical. If they went ahead and introduced it, then we would have a major burden to try to keep it off the market.

Mr. MOFFETT. I believe the industry when they say they are trying to be responsible. They said they have no intention of reintroducing unless they get the OK.

Mr. JELLINEK. They did not say that.

Mr. MOFFETT. They said it very clearly.

Mr. JELLINEK. They said it today. They did not say that to us.

Mr. MOFFETT. OK. They said it today very clearly. It is unmistakable that they want to be responsible. I believe them. They are not about to start marching on this thing again unless they get an OK from you.

If they did not get an OK from you, if you just said, "Look, I have consulted with all these other agencies; we have done this; we have done that. We cannot seem to come to an agreement here. We are very sorry. This is just one of those things, but there seems to be just enough risk to keep us from saying go ahead," they are not going to go ahead.

Mr. JELLINEK. I think that is right.

Mr. MOFFETT. If not, what is your regulatory burden?

Mr. JELLINEK. There would be no burden on us in that case.

Mr. MOFFETT. Then this whole assumption here of, "We had to make a decision not to regulate"—

Mr. JELLINEK. I did not say we had to make a decision not to regulate. I said we made a decision not to regulate.

Mr. MOFFETT. Right. Then maybe you made a mistake.

Mr. JELLINEK. I do not think we did.

Mr. MOFFETT. The whole thing just does not stand up.

Mr. JELLINEK. I do not understand your point.

Mr. MOFFETT. It does not stand up because you are proceeding on an assumption that if you do not make this decision that says, "OK, go back into the market with this," then the implication of what you were saying—and you were shaking your head when I was describing it as such—is that you want to be able to go on to more serious things, things that are known dangers and so forth. The implication is that this somehow handicaps you if you do not come down with this decision in terms of your regulatory burden, in terms of allocation of your resources. I simply do not think that is the case based on what we have heard.

Mr. JELLINEK. That was the assumption that we made as we considered that if we decided to regulate it, it would take us a

significant amount of time and resources to do it. We did not go ahead with the assumption that if we said to P. & G., "We have reviewed it and it is low risk but forget it. We are not going to say anything"—we did not assume if we did that then they would not manufacture it.

Mr. MOFFETT. OK. Then a new set of circumstances comes out today. Right? This is news to you. Therefore, maybe we had better go back to the drawing board and just reevaluate this whole thing. You were obviously proceeding on the basis of certain kinds of assumptions about what your burden would be if you did not come down with this decision. Now by your own admission there is new information here.

This industry obviously is not about to defy an agency. They are obviously not about to march ahead and go back into the market with this stuff even though they are convinced—and I believe they are sincere on this—that the stuff is safe. They are not about to do it unless they get the OK. They want the okay not only from you, but they are even saying now that they want to check with other agencies and so forth. They do not want to make a mistake. I think that is admirable.

Then your decision, I think, really needs to be questioned not only by us but by yourself, based on this. The fact of the matter is if you came out and said, "Well, there is not really a consensus here. It is getting close to a consensus but it is not quite a consensus. There is a debate in the scientific community."—if we would just say that and put this thing on hold for a little while longer or maybe elevate it into a full-blown rulemaking proceedings, at least allow public hearings, then in fact we are not jeopardizing anything really. We are costing the industry a little bit of time but hopefully they will be understanding about that.

Do you see what I am getting at? I am very sensitive to your point that you have limited resources. I want you to have more resources if you are doing the job well. I have fought for it in the past, and I will continue to fight for it.

Mr. JELLINEK. I understand that, and I appreciate it.

Mr. MOFFETT. I think the agency is undermanned. I do not think we are spending enough in a productive way on these problems, but this does not have a great deal to do with that. It really does not. That is the thread that goes through your entire testimony—that somehow you had to make a decision not to regulate because the opposite of making a decision not to regulate was a decision to regulate.

What we have done here today is to just disprove that was the case, with the help of some very good witnesses from the industry who were very candid with us. Therefore, I think we really ought to go back to the drawing board on this thing.

Mr. Chairman, I want to say this to you so that we have some continuity in this hearing: It seems to me that EPA made a decision to move ahead, a decision they term a decision not to regulate. The implication was and the testimony seems to reflect their belief that that decision had to be made because if they did not make that decision their resources would have to be channeled into this as opposed to something more important.

The fact of the matter is that EPA was assuming that the industry would not necessarily withhold these things from the market if they did not make a decision. That was the kind of pressure that they felt. I am not saying that it was an unwarranted pressure, but they in a way brought it upon themselves.

What Mr. Jellinek now tells us is the case that he was not aware that the industry was making a commitment not to move forward unless they got the OK from EPA. He was not sure, in other words, that the industry would not move forward anyway.

Mr. MAGUIRE. If you had been the industry, would you have displayed your hand on that particular point? Probably not.

Mr. MOFFETT. I do not know. All I know about the industry's motivation is I believe what they say today when they say they needed to get an OK and they had no intention of moving ahead without the OK from EPA. EPA made a decision not to regulate based on this business of resources.

Mr. Chairman, I think they ought to reconsider that decision, given the fact we have a very reasonable industry here that has no intention, apparently—and I applaud them—of moving ahead until they get the necessary OK's. The EPA decision was based in part on this business of allocation of resources and some pressure that they felt to come down with an affirmative decision on this, the opposite of which would have been, in their minds, a decision to put a whole regulatory apparatus into motion.

I wanted to leave you with that.

Mr. JELLINEK. The implication of the way you have summarized EPA's decision is that we "gave the chemical an OK." We did a risk assessment, which we concluded was low risk.

Mr. MOFFETT. Fine. How do you think it will be read? How would you read it if you were Procter & Gamble? Attribute the best motivation to Procter & Gamble. How would you read it?

Mr. JELLINEK. I think you ought to ask that of Procter & Gamble. They do not agree with our risk assessment as far as I can tell. They think there is no risk.

Mr. MOFFETT. Would you say that their testimony reflects the fact that they think it is OK if the Surgeon General and others tend to come down with the same kind of risk assessment that you made? Is that a fair characterization of their testimony?

Mr. JELLINEK. I refer you to their testimony. I sat here. They said they think it is safe. They do not think it is a carcinogen. We think it is a carcinogen. We think it is a low risk carcinogen.

Mr. MOFFETT. The bottom line for us is whether this stuff is going to go back on the market and whether we are fulfilling our responsibility in acquiescing or whatever. I do not know the answer to that, but I think it is clear that this was viewed as a green light by the industry, at least from you. Maybe they have a couple more green lights.

Mr. JELLINEK. I do not think anybody on the panel here asked them what they intend to do.

Mr. MOFFETT. Oh, sure we did.

Mr. JELLINEK. No one ever asked them directly what they intend to do based on this letter from me. We did not endorse it. We did not say it was safe. We said it was low risk.

Mr. MOFFETT. Let's ask you what is the effect in your view of this advisory opinion. Do you favor the stuff going back on the market or not?

Mr. JELLINEK. We have not reached that question.

Mr. MOFFETT. You have not reached the question?

Mr. JELLINEK. No. We have not done a risk-benefit analysis. We did a risk analysis.

Mr. MOFFETT. Is it possible that you are against its going back on the market? How will we ever know, Mr. Jellinek, what you do think?

Mr. JELLINEK. We do not think it is a high enough priority to make a risk-benefit decision on whether or not the chemical should or should not go on the market. I am really not splitting hairs here. We did a risk assessment. On the basis of the risk assessment we decided that it was low risk and not worth investing the kind of resources it would require to do a risk-benefit decision.

Mr. MAGUIRE. Do we understand then that you see your position as different from that of P. & G., at least as you read their testimony? I should include Monsanto as well. Your contention is that you do recognize that it is a carcinogen, that it does have some level of risk, whereas your understanding is that they do not think it has any risk. I think you said that you felt they did not think it was a carcinogen. Frankly, that was not my understanding of their testimony.

Mr. JELLINEK. It was a threshold.

Mr. MAGUIRE. I thought they said they recognized it was a carcinogen in laboratory animals at certain dosages.

Mr. JELLINEK. I stand corrected.

Mr. MAGUIRE. They rejected the notion that it was a substance that would have any carcinogenic effect in human populations at anything like the levels that it would be present in the environment. That was my understanding.

Mr. JELLINEK. I think that is correct.

Mr. MAGUIRE. Do either the representatives of P. & G. or Monsanto wish to make a statement at this point about what they plan to do with respect to the marketing of NTA, given Mr. Jellinek's statement that we failed to get an answer on that point when they were before the committee? Do either of the representatives wish to comment on that?

Mr. THRODAHL. I think it is inappropriate for me to respond to that without the Procter & Gamble people here. We can give you an answer at a later time. I think it is inappropriate now.

Mr. MAGUIRE. Is there a representative from Procter & Gamble here? Are you in a position to comment on that?

Mr. COWAN. My name is Douglas Cowan. I was sworn in earlier.

In fact, there was no decision made. I think it is fair to say it was our intention as a company to continue to get consensus and conviction around our point of view and that the EPA was an important element in that. There were other elements—the Surgeon General's office. At any point we could have felt more encouraged or less encouraged, but to my knowledge we literally had not made a decision with respect to marketing.

Mr. MAGUIRE. You have not made it as of this minute, to the best of your knowledge?

Mr. COWAN. That is correct.

Mr. MAGUIRE. Is that the situation at Monsanto now that P. & G. has spoken?

Mr. THRODAHL. I beg your pardon?

Mr. MAGUIRE. They say they have not at this moment made a decision.

Mr. THRODAHL. I tried to explain at the time I was in the witness chair that Proctor & Gamble and other soapers are our customers. If they have not made a decision, then we have not made a decision.

Mr. MAGUIRE. That clarifies the relationship very well.

Mr. THRODAHL. You have to understand that.

Mr. MAGUIRE. Yes, I do. I said it clarifies it. Absolutely.

Does the gentleman wish me to yield further?

Mr. MOFFETT. Only to make a plea, Mr. Chairman, that we get some clarity. I thought about midday that there was more clarity here from EPA than I think there is now.

I would really be a little confused if I were part of the industry, let alone part of the subcommittee, over exactly what they are saying. We do not need to muddy the waters at all.

We need to make a determination here of what EPA intends to do from here on. Is this the end of it as far as you are concerned, Mr. Jellinek?

Mr. JELLINEK. Unless new data is introduced. Let me put it this way: As far as the EPA is concerned, if they go ahead and introduce the chemical, we do not intend to take any action to limit that introduction unless new data develops that would change our risk assessment.

That is why we wrote the letter expressing our concerns and expressing our recommendations on monitoring and environmental studies. If those monitoring or environmental studies turn out to raise questions, then we will take regulatory action.

I might add that our recommendations for them to do those studies were done in an informal manner, but we are fully prepared to require those studies to be done if the industry does not cooperate voluntarily.

Mr. MOFFETT. I understand that. Here is what bothers me. One thing that bothers me is that it seems to me the industry is trying harder to get a consensus out of the Government than you are. It is really ironic. They are saying, "Yes, we do not want to make a mistake. We are going to go to the Surgeon General. We are going to ask this agency and that agency." You did not even do that.

Mr. JELLINEK. I think there is some confusion about that. The fact is that the national toxicology program which includes every health research agency of note in this matter and which reports to the Surgeon General and which includes a representative of the Surgeon General did a detailed review of the carcinogenicity of this data, and in terms of the risk came up with a conclusion consistent with that of EPA. As a matter of fact, their estimate of risk was lower than EPA's.

Mr. MAGUIRE. But they did not make the functional equivalent of a regulatory decision.

Mr. JELLINEK. That is not their job.

Mr. MAGUIRE. Nor did they know about the one that you announced on the 27th of May, nor were they permitted to comment on it as to whether they thought it made sense or not.

Mr. JELLINEK. As Dr. Rall said in his testimony, he agreed with our risk assessment and it is not his job to make the policy decisions.

Mr. MAGUIRE. I got the impression from his testimony that he was very uncomfortable about the functional equivalent of a regulatory decision that you have in fact made, as were other witnesses. Did you get that impression?

Mr. JELLINEK. No, I did not. I got the impression that it is not his—that he stayed away from that. That is not his role. Frankly, I question whether research agencies want routinely to get into the business of making regulatory decisions.

Mr. MAGUIRE. When Mr. Beck was before the Health and the Environment Subcommittee I got the impression that he was very uncomfortable with the decision.

I would like to ask the gentleman from P. & G. a question. Do you intend—"you" meaning P. & G.—to consult with the Surgeon General on this? I think I heard you say that. Is that correct?

Mr. COWAN. I do not want to leave in the record an impression we were going to ask everyone's opinion. In other words, what we were trying to do was to get a clear definition from EPA of the risk assessment. If the risk assessment had been extremely reassuring, then I do not know who else we would have consulted.

Mr. MOFFETT. Mr. Chairman, with all due respect, the P. & G. people this morning indicated, in response to several questions from me, that they intended to consult.

I want to go back to the consulting of EPA. What was Mr. Costle's role in this, if any?

Mr. JELLINEK. He was informed of our proposal.

Mr. MOFFETT. Did he check off on it, so to speak?

Mr. JELLINEK. He checked off on it.

Mr. MOFFETT. Was there any White House involvement in this?

Mr. JELLINEK. No.

Mr. MOFFETT. None whatsoever?

Mr. JELLINEK. No.

Mr. MOFFETT. What about legal advice? Was there legal advice? Did you seek legal advice on the question of whether you should have gone the formal route or whether this advisory opinion was satisfactory?

Mr. JELLINEK. No; we didn't.

Mr. MOFFETT. Therefore, you do not have any legal opinion that you could share with us with regard to whether or not you were in compliance with TSCA, for example?

Mr. JELLINEK. No; I do not. We do not have an opinion. I wish we had.

Mr. MOFFETT. I am sure you do.

Mr. MAGUIRE. Mr. Jellinek, are you concerned at all about the possibility that a precedent may have been set here which might not be a wise one for the future; namely, that this process you described can be entered into apart from the requirements of the

law and the usual administrative procedures in order to get the functional equivalent of a regulatory decision?

Mr. JELLINEK. No; I do not think it is precedential. As I described, there were some unique circumstances. We just do not do this kind of thing normally.

Mr. MAGUIRE. You are not going to do this again?

Mr. JELLINEK. Not in the normal circumstances I can conceive, although things might come up.

Mr. MAGUIRE. If it was valid to do it in this case, why isn't it valid to do it in other cases?

Mr. JELLINEK. It was a matter of reasonableness and fairness. The Government persuaded the industry to take the chemical off the market. The industry came back and said, "A lot has happened in the past 10 years. Would you look at this again and tell us what you think?" We thought that was a reasonable thing to do.

Mr. MAGUIRE. Is this the only example of a situation in which there has been voluntary restraint by industry at the behest of Government?

Mr. JELLINEK. It is the only one that I know about that might fall under TSCA. In the pesticide area we routinely persuade companies to drop pesticides voluntarily. I assume if new data came up on those pesticides and we were asked to review the situation again, we would.

Frankly, we like to get chemicals that we are concerned about off the market voluntarily if at all possible. It is a lot more cost-effective in terms of our own resources.

Mr. MAGUIRE. Is there a case recently in which manufacturers of asbestos have made inquiries to your office, specifically to one of your deputies, about the possibility of a letter similar to that which you provided on the 27th to Procter & Gamble?

Mr. JELLINEK. I do not know of any, but the facts in that situation are different, to say the least.

Mr. MAGUIRE. Is Mr. Muir here to clarify that point?

Mr. JELLINEK. Let me say that even more clearly. Not only are we not considering anything like that, but asbestos is one of the chemicals that we are spending a lot of time working on, looking toward regulations. We already put out an advanced notice of proposed rulemaking. We are working on two proposed rules which will be out within the next 6 months to regulate asbestos.

Mr. MAGUIRE. Is Mr. Muir here? Could you tell us what you know, if anything, about this matter that I just raised?

TESTIMONY OF WARREN R. MUIR, DEPUTY ASSISTANT ADMINISTRATOR FOR TESTING AND EVALUATION, OFFICE OF PESTICIDES AND TOXIC SUBSTANCES, ENVIRONMENTAL PROTECTION AGENCY

Mr. MUIR. Nothing. It would be very interesting.

Mr. MAGUIRE. You know nothing about it?

Mr. MUIR. No.

Mr. JELLINEK. This was the asbestos industry people asking us for a similar letter or asking us for a similar review?

Mr. MAGUIRE. Mr. Muir, would you come forward? We would like to swear you in.

Do you swear to tell the truth, the whole truth, and nothing but the truth, so help you God?

Mr. MUIR. I do.

Mr. MAGUIRE. Mr. Segal?

Mr. SEGAL. I just want to clarify something for the record. At the time there was a briefing of staff that included Mrs. Jacobson and myself, you were asked whether there were other chemicals like NTA. You said right after the NTA decision people from the asbestos industry had come by. At this point I hope that recollects the situation enough for you to tell us your perception of what happened.

Mr. MUIR. I recollect the discussion.

We have never been requested by the industry to endorse asbestos. All I indicated was that in the course of a meeting with asbestos industry executives, that they had noted the assessment that we had made on NTA and the letter that we had sent out on it. They indicated to us that they were sure when we carried out our assessment on asbestos that we would find that the risks were indeed lower than that which occurred with NTA. At no time did they request an endorsement of asbestos. That is clearly not the posture that the agency is in.

We have published an advanced notice of proposed rulemaking concerning asbestos. We have a very heavy commitment to regulatory action toward asbestos.

Mr. SEGAL. However, they did in fact cite the letter that you sent on NTA as a precedent, if you will, for EPA taking some action along these lines; is that correct?

TESTIMONY OF STEVEN D. JELLINEK—Resumed

Mr. JELLINEK. I think you are misunderstanding that. From what Warren told me after the meeting, just as he told you in the briefing, they said they think the risks are going to be lower with asbestos than with NTA. That is their opinion. Although we have not completed our risk assessment yet, we do not agree with that.

Mr. SEGAL. We understand that. The question is did they use the NTA letter to Procter & Gamble and Monsanto as a precedent for saying EPA can look at an issue along the lines that you looked at the NTA situation. We are not talking about the relative risks.

Mr. JELLINEK. I do not interpret it that way. If somebody had said at a meeting that NTA risks were low, then one of the asbestos executives might have come up and said, "Well, you will find that our risks are even lower." That is their opinion. As Warren said, we are heavily involved in regulatory action on asbestos.

Mr. MAGUIRE. Was the EPA cancer-risk assessment group involved in the decision that you made?

Mr. JELLINEK. The group was not involved in the cancer-risk assessment of NTA, but the risk assessment was made using the procedures of the cancer-risk assessment group.

Mr. MAGUIRE. In EPA you have a cancer-risk assessment group?

Mr. JELLINEK. That is right, but we do our own cancer-risk assessments in the Office of Pesticides and Toxic Substances for the most part.

Mr. MAGUIRE. Would it not have been appropriate for the cancer-risk assessment group of EPA to have been consulted about a

decision to allow 1 billion pounds, plus or minus, of cancer-causing substance into the water supply?

Mr. JELLINEK. It was not necessary; it might have been appropriate. We used their procedures. We did the risk assessment the way they do risk assessments. We do our own risk assessments for the most part in my office. They provide an oversight, quality control role.

Mr. MAGUIRE. Did they provide an oversight quality control role in this instance?

Mr. JELLINEK. Not in this particular instance.

Mr. MAGUIRE. Why not?

Mr. JELLINEK. Their's is a broader function. They design procedures for the agency to use in performing risk assessments. They do not review every one of our risk assessments.

In hindsight I wish that we had consulted with them, although I do not think the result would have been any different.

Mr. MAGUIRE. Not only did we not have any formal signoffs from the Surgeon General or the Division of Drinking Water Resources or NIEHS, but we also did not even have a reference of this matter to EPA's own cancer-risk assessment group.

Mr. JELLINEK. I will agree to that with the modifications and clarifications in my response to you.

Mr. MAGUIRE. You have said before that none of the benefits were evaluated by you. That is, you did not look at the question of whether NTA was the equivalent of or superior to in relation to carbonates or any other alternative detergent ingredients; is that correct?

Mr. JELLINEK. That is correct.

Mr. MAGUIRE. However, you would agree that any risk-benefit assessment worthy of the name would have to include that kind of determination of the benefits?

Mr. JELLINEK. That is correct.

Mr. MAGUIRE. Under the situation as we now have it, I take it that the benefits are going to be calculated and decisions about whether the detergent is going to have this ingredient in it or not are going to be made by those who manufacture and produce it; is that correct?

Mr. JELLINEK. I do not know.

Mr. MAGUIRE. You have not done it; is that right?

Mr. JELLINEK. That is right.

Mr. MAGUIRE. To the best of your knowledge, no other agency of Government has done it?

Mr. JELLINEK. That is right.

Mr. MAGUIRE. Therefore, the industry that produces the ingredients presumably is going to do the best job they can of that. Would that be your assumption?

Mr. JELLINEK. I assume so. As they have testified, they believe there are benefits.

Mr. MAGUIRE. Suppose just hypothetically there were only the most marginal benefits and you had on your table indications that on the one hand the benefits were marginal and on the other hand that there was a risk of cancer, as you have earlier testified. What would you say then about the advisability of including that material in a marketable product of the sort we are discussing?

Mr. JELLINEK. I do not like to speculate. Generally, when we do make risk-benefit decisions, if the benefits are marginal or very low we tend to be concerned about the risks.

Mr. MAGUIRE. Yet you went through a procedure which eliminated your participation in an analysis of those benefits and their degree of marginality or indeed in any final balancing or evaluation of the risks and the benefits at that point. Is that correct?

Mr. JELLINEK. That is correct. The reason for that was we did not believe that the risks were high enough to devote the time and resources that would be required to do the benefit analysis.

Mr. MAGUIRE. Would that have been the case even if the benefits were zero?

Mr. JELLINEK. We would have had to conclude that the benefits were zero by doing the work. We decided not to do the work.

Mr. MAGUIRE. Therefore, you were willing to accept the risk with all the uncertainties that were included in your analysis plus all the uncertainties that you heard expressed by various expert witnesses this morning, which presumably you analyzed in the process of doing your analysis, despite the fact that you had no knowledge as to whether there were any significant benefits or indeed any benefits involved on the benefit side. Is that right?

Mr. JELLINEK. We had less uncertainty about the risk than some of the witnesses today. We feel very certain that the risks are low.

Mr. MAGUIRE. Are you at EPA in the habit of editing and altering independent, or supposedly independent, analyses which you contract out, along the lines suggested by those in a company whose process or product is being evaluated?

Mr. JELLINEK. I would rather not generalize. If you are talking about a specific instance, I would be glad to try to answer the question.

Mr. MAGUIRE. There were some 79 recommended changes offered by P. & G. to a draft report done for EPA by Midwest Research Institute. Some of them at least led to revisions of the report entitled "Potential Worker and Consumer Exposures to NTA in Detergents."

Is it a fact that some revisions were made pursuant to the proposed revisions offered by P. & G.?

Mr. JELLINEK. Let me try to put some perspective on that report.

Mr. MAGUIRE. First of all, what is the answer? Were they or were they not made?

Mr. JELLINEK. I will assume they were.

Mr. MAGUIRE. They were?

Mr. JELLINEK. Yes. The data on consumer and worker exposure was developed by P. & G., and I assume by Monsanto, based on their experience. They are the only people that we knew that had any data on these exposures.

Prior to our risk assessment no one who had done any risk assessments in the past had done assessments on anything but drinking water exposure. We went the extra step and did the exposure work on consumers and workers. Part of that data was given to us by P. & G. It was, in turn, given to a contractor to evaluate and do the exposure assessment.

It is common and I think reasonable, to give draft reports to those who generated the data in order to comment on the use of

that data, in the report, particularly when that data was supplied voluntarily by the industry in question.

There is an implication of impropriety in your question which, frankly, I do not accept.

P. & G. gave us the data at our request. We gave the data to our contractor. Our contractor came up with a draft report. We gave our draft report to P. & G. to look at. They had comments on the data that they provided. We took some of those comments; we rejected others. The draft report was turned into a final report. As I said before, this is the first time anybody had done an assessment of consumer or worker exposure for NTA.

I might add that, fortunately or unfortunately, regulatory agencies are dependent upon the industry for much of the data that we have to use in our decisions. If we had not gotten the data that we got voluntarily and had wanted it, we could have gone into a formal rulemaking.

I might also add that the draft report was reviewed by others inside EPA, and by a member of the International Joint Commission Task Force on the Health Implications of NTA.

Mr. MAGUIRE. Was it reviewed by anyone outside EPA other than P. & G.?

Mr. JELLINEK. I think it was. Yes, it was.

Mr. MAGUIRE. The Canadians?

Mr. JELLINEK. The IJC. It was not sent to Canada.

Mr. MAGUIRE. Are these Ms. Welch's notations which say "OK," "OK," "OK," et cetera, in the margin in the letter to Ms. Welch from Procter & Gamble? Are those Ms. Welch's notations on what was going to be wrapped into the report?

Mr. JELLINEK. Ms. Welch is here if you would like her to answer that question.

Mr. MAGUIRE. Ms. Welch, would you come up to the table, please?

Would you stand and be sworn?

Do you swear to tell the truth, the whole truth, and nothing but the truth, so help you God?

Ms. WELCH. I do.

Mr. MAGUIRE. Are those your notations?

Ms. WELCH. May I see the letter?

Yes, sir, I think they are.

Mr. MAGUIRE. How many of the proposed 79 changes made by P. & G. ended up in some form in the final document?

Ms. WELCH. I do not recall a number. It is fair to say that the reasonable changes that they asked for were included. There were a number of inaccuracies that occurred in the first draft of the contractor's report. After thoroughly reviewing that report, Procter & Gamble came up with some things that were in that report which were not accurate. I felt it prudent to change the inaccuracies in the report or to request that we revise that draft so that it would be a good document.

Mr. MAGUIRE. Did you do the revisions?

Ms. WELCH. Did I do the revisions?

Mr. MAGUIRE. Yes.

¹ Justine Welch, biologist, Assessment Division, Office of Toxic Substances, Environmental Protection Agency.

Ms. WELCH. The contractor did the revisions.

Mr. MAGUIRE. You sent this document to the contractor saying which ones you thought were OK and which were not?

Ms. WELCH. I suggested places in the document that required further review by their in-house experts.

Mr. MAGUIRE. You also noted that a number of them were OK with you?

Ms. WELCH. That they seemed reasonable to me, yes.

Mr. MAGUIRE. Did you involve yourself in discussions with P. & G. or the contractor about whether the workplace atmosphere involving dust and so on as a result of spills or other malfunctions could be described as abnormal events or whether they were perhaps not best described as abnormal events?

Ms. WELCH. I do not recall.

Mr. MAGUIRE. We will include these various documents at this point in the record.

[Testimony resumes on p. 296].

[The documents referred to follow:]



THE PROCTER & GAMBLE COMPANY

MIDDLETOWN TECHNICAL CENTER

April 27, 1979

CINCINNATI, OHIO 45202

Ms. J. Welch
Hazard Assessment Group
Office of Toxic Substances
U.S. EPA
401 M Street, S.W.
Washington, D.C. 20460

Dear Ms. Welch:

This letter transmits Procter & Gamble's comments on the following draft report:

"Task IV - An Investigation to Assess and Predict Potential Worker and Consumer Exposures to Nitrilotriacetic Acid (NTA) in Detergents", report by Midwest Research Institute (MRI) to EPA.

Draft Final Report, March 9, 1979

EPA Contract No. 68-01-3896
MRI Project No. 4441-L

By way of background, Dr. Thomas Lapp of MRI called me on April 9, 1979 to indicate that EPA was interested in having Procter & Gamble's comments on this draft report, that he would send me the report to review, and that Procter & Gamble's comments should be sent to you with a copy to MRI (Dr. Lapp). For purposes of record, I confirmed this with you during an April 23 phone conversation, indicating that I had received a copy of the report from Dr. Lapp.

Attached is a copy of the report upon which specific comments have been made. Each comment is numbered, and the rationale for each is given below:

- 62 ✓ 1., p.1. This suggested wording more correctly reflects the actual situation.
- 62 ✓ 2., p.2. One should consider worker exposure to all process chemicals, not just those that are "toxic", since hazard to workers is a function of both exposure and toxicity.
- 62 ✓ 3., p.4. The process for making granular laundry detergents involves elements of both batch and continuous processes; this suggested wording change more accurately reflects the actual situation.
- 62 ✓ 4., p.4. Part of the process for manufacturing granular laundry detergents involves surfactant making via chemical reactions; hence this suggested wording better reflects the actual operation.
- 62 ✓ 5., p.4. Liquid laundry detergent and powdered cleanser manufacture can also involve elements of both batch and continuous processes.

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6., p.4. This paragraph highlights only negatives, things that potentially can happen but are not normal. It does not give fair weight to the highly automated, closed system nature of detergent manufacture which results in minimal worker exposure, and to the history of safe operations associated with detergent manufacture. Additionally, worker exposure during normal operations and atypical situations such as spills, equipment cleanup and so forth, can be controlled to the extent necessary via protective clothing and equipment. Furthermore, the same type of atypical situations can result from the manufacture of NTA itself, and these were not highlighted in such manner in the "Analysis of Probable Worker Exposure" paragraph on p. 3.

Consequently, the following rewording of this paragraph is suggested:

"Workers potentially could be exposed in the event of spills, equipment malfunctions, or equipment cleanup operations. However, the automated nature of detergent manufacture in closed systems normally leads to minimal exposure. In this situation and in atypical cases such as spills, worker exposure can be controlled to the extent necessary by protective clothing, equipment and proper procedures."

OK 11., p.5. Procter & Gamble believes a figure of 1500 workers is more correct when considering granular laundry detergent manufacture. The 2500 figure would be appropriate when considering granular and liquid laundry detergent, and dishwashing detergents. If the 2500 figure is used, then the wording of this sentence should indicate this includes both laundry and dishwashing detergent manufacture.

OK 12., p.5. This provides more correct wording and acknowledges the fact that exposure via airborne dust has been estimated rather than actually determined by measurement. The added sentence provides the assumptions in the estimates.

OK 13., p.5. This is a suggested wording improvement.

OK 14., p.5. This provides more complete information.

OK 15. and 16., p.5. NTA itself would not be used as an automatic dishwashing or light duty detergent, but would be formulated with other ingredients to make the finished detergent product. This suggested wording change better reflects the actual situation.

OK 17., p.6. The change from "adult female" to "70 kg adult" more correctly reflects the basis of the estimate. The estimated exposure from residual NTA on clothes is 0.018 $\mu\text{g/kg/day}$, not 0.18 $\mu\text{g/kg/day}$ as given in Dr. R. E. Winters' November 10, 1978 letter to Ms. J. Welch of EPA. This correction was noted in Mr. W. D. Hopping's December 11, 1978 letter to Ms. Welch. A copy was sent to Mr. R. Reisdorf of MRI.

OK 18., p.11. This wording more completely states what actually was done. Also, the analytical test measures anything that releases formaldehyde in acid, and hence gives an upper limit to formaldehyde content of commercially produced NTA.

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- OK 15, p. 12 This acknowledges the limitation of the analytical test.
- MRI 16, p. 16. This wording recognizes the fact that worker exposure can be controlled in the event of spills, leaks, etc. *can't?*
- OK 17, p. 18. This again acknowledges analytical limitations for formaldehyde measurement.
- MRI OK 18, p. 19. The lowest value given by Monsanto in Table I of their report is < 1.69 mg, not < 1.85 mg. *? B+A don't say that*
- 19, p. 19. There is confusion here between "metabolism" and "absorption". The Monsanto report (Hill et al., 1977) equated metabolism with absorption, while MRI is using metabolism to mean biotransformation. There is substantial evidence, including the cited Budny and Arnold (1973) paper, which conclusively demonstrates that NTA undergoes ~~no~~ biotransformation in the body. All NTA absorbed by the body is excreted unchanged in the urine, and NTA entering the body but not absorbed is excreted unchanged in the feces. *This has been demonstrated in humans, rabbits, dogs, monkeys, mice, and rats. For NTA dosed via IV infusion to rats, all NTA appears unchanged in the urine. In chronically fed rats, there is greater than 97% assurance that no biotransformation occurs; 2-dimensional TLC shows identical results for the NTA fed and material isolated from urine.*
- II - should* Consequently, "metabolized" in line 11 of p. 19 should be "absorbed" to be consistent with MRI's usage, and the footnote at the bottom of p. 19 is in error and should be deleted. The point of the inhalation exposure is that even if all of the total 0.1 to 0.5 mg NTA exposure during an 8-hr shift were absorbed, the concentration of NTA in the urine would be below the detection limit of 0.5 mg/l. *is this true?*
- OK 20 and 21, p. 26. These changes, as discussed under comments 3 and 4, more correctly reflect the actual nature of the manufacturing process.
- OK 22, p. 26. The wording change to "currently averages 15% in Canada" more correctly indicates the actual situation. The mention of a phosphorus limit is superfluous and can be deleted. *NO - quite imp. for perspective*
- OK 23, p. 26. As mentioned in comment 5, this change more correctly describes the nature of the process.
- MRI 24, p. 26. The statement that powdered cleansers would contain less than 1% NTA is unfounded speculation and is best deleted. *is it??*
- MRI 25, p. 26. No support is given for the statement that filling and packing of cleansers are major sources of dust; how does MRI know this is true? In this operation, worker exposure is controlled to whatever extent is necessary. *is this true?* Deletion is suggested.
- OK 26, p. 26. As with comment 5, this wording change better reflects the actual process.

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- OK ✓ 27., p. 27. The comments and suggested rewording under comment 6, p. 4 are made here.
- MRE → 28., p. 27. Comment 7, p. 5 is made here.
- I check 28., p. 27. Reference to R. E. Winters is incorrectly cited (see references for Section 4, p. 31).
- OK ✓ 30., p. 28. Deletion of "detergent" more correctly indicates that total dust was measured. *No - OK as is*
- OK ✓ 31 and 32., p. 28. Reference to R. E. Winters is incorrect (see references for Section 4, p. 31).
- OK ✓ 33., p. 30. The Procter & Gamble calculations are estimates, and are not actual measured values.
- OK ✓ 34., p. 30. Procter & Gamble prefers not to identify the Hamilton, Ontario plant. One can simply state "a plant" without losing anything.
Should indicate it is a plant or actual experience - because Hamilton plant
- MRE ✓ 35., p. 30. The 1978 reference to Hopping is incorrect (see references for Section 4, p. 31).
- MRE ✓ 36., p. 31. These are suggested changes and corrections for the references.
- I check → 37., p. 34. The date of the reference to R. E. Winters is incorrect (see references for Section 5, p. 49).
- No ✓ 38., p. 35. This most certainly represents a very small exposure. The automatic dishwashing detergent is in a box which typically has a foil wrapper; thus there is minimal potential for skin contact. Additionally, the detergent is normally poured directly into the machine's detergent receptacle, thereby offering an extremely low potential for dust generation, and only a short, perhaps 10 sec., exposure time. Although a potential does exist for exposure while pouring and handling, it obviously is very, very small.
p. 35 addresses # of people exposed, not extent - a comment addressing # would be in p. 36
- OK ✓ 39., p. 35. There is no need to indicate that the industry source wished to remain anonymous; this statement can be deleted.
- OK ✓ 40., p. 35. A suggested wording improvement.
time
- No ✓ 41., p. 36. It is not virtually certain that persons owning an automatic dishwasher would also wash dishes by hand at some time, even though this is likely. The suggested change reflects this.
I think it is
- No ✓ 42., p. 36. These suggested changes more correctly reflect the actual data (i.e. number of households) and the assumption used (i.e. 1 person/household does dishes). *this P and G revised up my comment*
- OK ✓ 43., p. 37. This provides more precise wording.

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of 46, p. 37. A suggested wording improvement.

OK 45, p. 39. The suggested change provides more precise wording.

46, p. 39. In laundry detergent, NTA would not be adsorbed on the surface of the granule, but rather would be distributed throughout the granule. The suggested rewording reflects this fact. *True?*

47, p. 39. This provides the correct reference to R. E. Winters (see references for Section 5, p. 49).

48, p. 39; 49 and 50, p. 40. Hendrick's studies simulated home use in the laboratory; they were not actual in home studies. The suggested rewording reflects this. *See 2. Consider the time delay and settle in - not time to empty a clothing bag*

51, p. 42. The assumption of a 2 min exposure time is extremely conservative, since this was the time required to empty an entire 49 oz. box of detergent by double-pour in the Colgate-Palmolive study. Obviously, it would take only a few seconds to pour and empty 1.25 cups, a typical usage per laundry load. A 49 oz. box of detergent contains 1389 gm (28.35 gm/oz) and at a typical density of 77 gm/cup, the box would contain 18 cups of detergent. With 2 min required to empty the entire box, a pouring rate of 9 cups/min can be calculated. For a usage of 1.25 cups, this would require 0.14 min or about 8 sec. Consequently, the exposures in Table 5 (p. 42) have been recalculated for an exposure time of 0.14 min. This provides a more precise estimate of exposure per laundry load, and is a more correct basis for comparison with the Procter & Gamble results. It also brings the NTA exposures estimated from the Procter & Gamble and Colgate-Palmolive data into better agreement, and is a suggested way of presenting the exposure data.

52, p. 43. Inhalation exposure with use of automatic dishwashing detergents would be less than that from laundry detergents. Firstly, the dishwashing detergent is normally poured directly from the box into the machine's receptacle, thereby providing minimal dust generation potential. Secondly, a normal usage per load (typically 1 load/day) is about 50 gm, or about 0.16 cup (2.5 tablespoons). Accordingly, the exposures estimated here are high by a factor of at least 6.25 (1 cup : 0.16 cup) for exposure per use. Furthermore, while a figure for NTA level in automatic dishwashing detergent must be assumed in making an estimate, it should be recognized that any figure, including the 25% used here, is both speculative and arbitrary. *from house print, but I think it's valid to use a max of 1 cup/day instead of typical. It is unrealistic to assume exposure to be reduced (i.e. divided) by a factor of 6.25, to more correctly reflect actual daily usage. This exposure estimate is still high because less dust generation will result from use of automatic dishwashing as opposed to laundry detergents.*

53, p. 43. This provides a correction to reference to R. E. Winters (see references for Section 5, p. 49).

54, p. 44. This identifies assumptions made in estimating the washwater concentration (see references for Section 5, p. 49).

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→ 83, p. 44. This provides more complete reference to the data (see references for Section 5, p. 49).

→ 84, p. 44. The decimal point is misplaced.

→ 87, p. 44. This provides a reference for the data (see references for Section 5, p. 49).

→ 88, p. 44. The decimal point is misplaced.

→ 89, p. 44. Importantly, the $0.25 \mu\text{g}/\text{cm}^2$ was the maximum observed.

→ 90, p. 44. While additional work would be needed to more precisely define NTA absorption through human skin, the data used do provide an upper limit, i.e. exposure to NTA at higher concentrations and for longer than expected, and rat skin permitting greater penetration than human skin.

→ 91, p. 45. This suggested rewording more correctly indicates that data was provided (not obtained) by Procter & Gamble to MRI, and provides the correct reference to the data (see references for Section 5, p. 49).

→ 92, p. 45. Exposure to detergent adhering to the container should be minimal. The detergent is inside the container, thereby precluding direct contact with skin. It is hard to imagine how significant exposure could occur to powdered detergent on the outside of the container, i.e. powdered detergent will not adhere to the container very well. Of course, liquid detergent could adhere better to the outside of the container.

In his 1970 paper, Hendricks provided information on detergent spills in the home. Of over 100 housewives interviewed, about 50% claimed never to have spilled laundry detergent. Of those that remembered spilling some, 80% reported that the amount spilled was no more than 1 cup, with the majority of these reporting a few granules or a few spoonfuls at most. These considerations, then, when coupled with the facts that one most likely would rinse the hands after direct contact with detergent and that the $0.25 \mu\text{g}/\text{cm}^2/\text{day}$ absorption value was the maximum measured over a 24 hr period in rats, whose skin is more permeable than that of humans, suggest that exposure in atypical situations such as spills would be very small.

→ 93, p. 45. The units on the concentration have been corrected.

→ 94, p. 45. This provides a more complete and correct reference to the data (see references for Section 5, p. 49).

→ 95, p. 46. This provides more complete and correct reference to the data (see references for Section 5, p. 49).

→ 96, p. 46. Suggested improvement in format. *not needed.*

→ 97, p. 46. The 8% absorption value used in Dr. P. E. Winters' November 10, 1978 letter to Ms. J. Welch is in error; the correct value is 0.8%. This correction

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was noted in Mr. W. D. Hopping's December 11, 1978 letter to Ms. Welch. A copy was sent to Mr. R. Reisdorf of MRI.

68., p. 46. This indicates the assumption made concerning NTA level in product when calculating its washwater concentration.

69., p. 47. These changes reflect the correct absorption value (0.8%, not 8%).

70., p. 47. The suggested wording reflects the fact that one is not virtually certain NTA is not used in dishwashing detergents.

MRI → 71., p. 47. This provides the reference for the data and calculation (see references for Section 5, p. 49).

72., p. 47. This corrects an arithmetical error.

73., p. 48. The product concentration in the actual wash phase of an automatic dishwasher cycle is about 0.3%. The wash phase is then followed by several hot water rinses and because of this, Procter & Gamble believes NTA deposition on dinnerware washed with an NTA-containing automatic dishwasher detergent would be less than that for hand wash and rinse. Also, automatic dishwashing detergents contain ingredients to provide "sheeting action", i.e. to prevent deposition and resultant spotting. This should further reduce NTA deposition on dinnerware. As mentioned previously, assumption of a 25% product level is speculative and arbitrary.

If one assumes 25% NTA in automatic dishwasher detergents, Procter & Gamble believes the exposures projected in the last paragraph represent an upper limit for the reasons given above. The suggested wording reflects this.

MRI → 74., p. 49. The changes made in the Section 5 references provide more complete and accurate citing of the data. The February 1, 1979 reference to Hendricks was not mentioned in the text of Section 5, and hence can be deleted.

True?
As a final comment, I want to again emphasize that potential use of NTA in liquid and automatic dishwashing detergents, and powdered cleansers is, at this point in time, speculative. Such use could or could not occur, depending on what future technology makes available. Furthermore, assumption of an NTA level in such products for purposes of making exposure projections is both speculative and arbitrary. The relationship of exposures so projected to what actually could occur in the future is not precisely known.

This concludes Procter & Gamble's comments on the report. We would be happy to meet with you and/or MRI scientists to discuss our comments and to provide any additional information which may be of use. Accordingly, please feel free to contact me.

Sincerely yours,

THE PROCTER & GAMBLE COMPANY

William D. Hopping

William D. Hopping
Packaged Soap & Detergent Division

kkk
Attachment
cc - Dr. T. Lapp - MRI (w/attachments)

Hopping

CHEMICAL TECHNOLOGY AND ECONOMICS IN
ENVIRONMENTAL PERSPECTIVE

TASK IV - AN INVESTIGATION TO ASSESS AND PREDICT
POTENTIAL WORKER AND CONSUMER EXPOSURES TO
NITRILOTRIACETIC ACID (NTA) IN DETERGENTS

DRAFT FINAL REPORT

March 9, 1979

EPA Contract No. 68-01-3896
MRI Project No. 4441-1

For

Environmental Protection Agency
Office of Toxic Substances
401 M Street, S.W.
Washington, D.C. 20460

Attn: Mr. Roman Kuchkuda
Project Officer

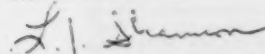
PREFACE

This report presents the results of a study to assess and predict worker and consumer exposure to nitrilotriacetic acid in detergents.

This study was performed by Midwest Research Institute, as Task IV, under Contract No. 68-01-3896 for the Office of Toxic Substances of the U.S. Environmental Protection Agency. The Office of Toxic Substances' project officer for this study was Mr. Roman Kuchkuda. Principal Midwest Research Institute contributors to this study included: Dr. Alfred F. Meiners (Task Leader), Principal Chemist; Mr. Charles Mumma, Senior Chemical Engineer; Dr. Eugene Podrebarac, Senior Chemist; Mr. Robert Reisdorf, Associate Occupational Health Scientist; Mr. Harold Owens, Associate Industrial Chemist; and Mr. Howard Gadberry, Senior Advisor for Technology. Mr. Albert E. Stewart, President, Stewart Industrial Hygiene Service, acted as consultant. Dr. Thomas W. Lapp is the project leader for this contract, under the supervision of Dr. Edward W. Lawless, Head, Technology Assessment Section.

Approved for:

MIDWEST RESEARCH INSTITUTE



L. J. Shannon, Executive Director
Environmental and Materials
Sciences Division

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NOTICE

This document is a preliminary draft. It has not been formally released by the U.S. Environmental Protection Agency and should not at this stage be construed to represent Agency policy. It is being circulated for comments on its technical merit and policy implications.

SECTION 1

INTRODUCTION AND OBJECTIVES

Nitrilotriacetic acid (NTA) is ^{being considered partial} ~~proposed~~ as a replacement for phosphates in detergents produced in the United States. Currently, NTA is manufactured by Monsanto and W. R. Grace, who export the material to the Canadian detergent market and supply it for use in certain industrial processes. Current Canadian household detergent products are estimated to contain up to 2% phosphorus. The NTA content of these detergents ranges from 0 to 25%; the industry-wide average of 15% is based on total poundage of detergent and the quantity of NTA sold in Canada.

The Environmental Protection Agency (EPA) is concerned about the possible consequences of NTA use in detergents in the United States. The purpose of this investigation is (a) to assess workplace (worker) exposure to NTA during manufacture and consumer exposure during use of detergents containing NTA, and (b) to predict the extent of worker and consumer exposure if U.S. production of NTA was increased to 1 billion pounds per year.

SECTION 2

SUMMARY

HUMAN EXPOSURE DURING MANUFACTURE

- The production of NTA is highly automated and is largely under remote control. Thus, production workers have little potential for exposure to ^{process} chemicals except in the bagging and loading operations of the final product, the trisodium salt of NTA.
- 2.

Production Technology

Trisodium nitrilotriacetate, the sodium salt of NTA, is currently being produced in the United States by Monsanto Chemical Company and by the W. R. Grace Company. The Monsanto plant, which has a production capacity of 100 million pounds annually, is reported to be operating at about one-half capacity. Monsanto apparently ships all of its product to Canadian consumers. The W. R. Grace plant is reported to have a production capacity of 40 million pounds per year, but is also operating at a reduced rate, approximately 50% of capacity.

The W. R. Grace production process involves three steps: (a) the reaction of formaldehyde and ammonia to give hexamethylenetetramine (HMT), (b) the reaction of hydrogen cyanide (HCN) with HMT to give nitrilotriacetonitrile, and (c) the hydrolysis of nitrilotriacetonitrile by sodium hydroxide to give trisodium nitrilotriacetate. The Monsanto plant also uses this process under a licensing agreement.

Based on information provided by W. R. Grace and Monsanto, a total of only 11 workers are estimated to be involved currently in production of NTA in U.S. plants. For a projected NTA production rate of 400 million pounds per year, an estimated labor force of 57 workers would be required. A rate of 1 billion pounds per year would require 98 to 120 workers.

Analysis of Probable Worker Exposure

The entire NTA production process is automated and all regular shift workers, except those engaged in product packaging and loading activity, are normally located in a remote control room, separated from the process operations. Air monitors located at various points in the plant area trigger an alarm in the event of any process leaks of toxic material.

Dust losses of product are apt to occur to the work atmosphere of the drying kiln, the product packaging area, and the product bulk loading operations. Therefore, the risk of worker exposure via both skin contact and inhalation appears to be greatest for these operations.

Worker Exposure Data

Actual worker exposure data have been compiled at the Monsanto facility. This study included representation of all job classifications in the plant. Urine samples were taken for analysis and the air in the breathing zone of each worker was monitored. NTA was not detected in the urine samples (detection limit, 0.5 mg/liter by gas chromatography/mass spectrometry (GC/MS)).

The highest exposure area, the hopper car loader area, had an average potential exposure of up to 10 mg NTA per 8-hr workday. In this area the workers normally wear protective clothing and equipment during periods of high exposure risk.

HUMAN EXPOSURE DURING DETERGENT FORMULATION

The Detergent Formulation Process

The use of NTA as a replacement for sodium tripolyphosphate in detergents would not require changes in the current manufacturing process in the United States.

The method currently being used for the commercial formulation of ^{granular} ~~syn-~~

3. ~~chemical~~ ^{laundry} detergents is ^{primarily} a batch process, in which raw ingredients are pumped or
4. conveyed through a closed system ^{mixers and} to mixers, and then blended into a slurry. The slurry is sprayed from the mixer into drying towers to achieve the desired granulation size and moisture content. The finished powder is then conveyed to production lines where it is automatically put into cartons and packed for shipping.

Liquid laundry detergents and powdered cleansers are also formulated by ^{primarily} ~~the~~ batch process in a closed system.

Areas of Exposure in Detergent Plants

The workplace atmosphere can become contaminated with detergent dust containing NTA from leaks in the product lines, spills caused by a malfunction in equipment, equipment cleanup operations, and from operations which require manual handling of bags of NTA. The filling and packing production lines can become high dust areas, particularly when powder is spilled as a result of machine jams and product changeovers.

Worker Exposure

The number of production workers that would be directly exposed to NTA from the manufacturing of detergents in the United States is estimated to be

7. 2,500. The use of NTA would not change the number of workers required to produce detergents at the present market level.

NTA via

9 Occupational exposure to airborne detergent dust (~~measured as respirable dust~~) in detergent formulation has been ^{estimated} ~~determined~~ to be $< 4.8 \mu\text{g/NTA per kilogram}$ per day for an adult male and $< 3.6 \mu\text{g/NTA per kilogram per day}$ for an adult female. This assumes that (1) all the dust is detergent, (2) NTA is 25% of the detergent, and (3) 10% of the dust is respirable.

CONSUMER EXPOSURE TO DETERGENTS

9 Consumer exposure to detergents ^{can} ~~usually~~ result from inhalation of detergent dust, percutaneous absorption from contact with wash water or direct skin contact with the detergent, ingestion of residue on dishes or utensils, and skin contact with residues in clothing.

Number of Consumers Exposed

Laundrying Operations--

The number of people in the United States that would be exposed to NTA while doing laundry has been estimated to be 174 million or 81% of the total population.

Dishwashing Operations--

10 An estimated 2 million households (~~persons~~) in the United States use laundry detergents for dishwashing by hand. ^{If each person in the household over 10 years of age washes dishes at sometime, a maximum of 5 million persons would be exposed.}

11 If NTA were used ⁱⁿ ~~as~~ automatic dishwashing detergents, an estimated 33 million persons would be exposed.

12 If NTA were used ⁱⁿ ~~as~~ light duty detergents, an estimated 174 million persons would be exposed since even those households with automatic dishwashers wash dishes (and other kitchen utensils) by hand at some time.

Residues in Clothing--

Virtually everyone in the United States would be exposed via this route.

Residues on Dinnerware--

An estimated 5.8 million persons would be exposed following hand washing of dishes with an NTA laundry detergent, 40 million persons exposed following dishwashing in an automatic dishwasher, and 214 million persons exposed following hand washing of dishes with a light duty detergent.

Extent of Exposure

15 ~~Figure~~ Consumer exposure to NTA from inhalation of detergent dust has been estimated to be 0.001 $\mu\text{g}/\text{NTA}$ per kilogram per day (^{70 kg adult} ~~adult male~~). Exposure to NTA via percutaneous absorption from washing dishes (or laundry, etc.) by hand has been estimated to be 0.13 $\mu\text{g}/\text{kg}/\text{day}$ (^{70 kg adult} ~~adult male~~) for a 1/2-hr exposure. The estimated exposure from ^{residual} NTA ~~residues~~ ^{on} clothes is ^{0.018} ~~0.018~~ $\mu\text{g}/\text{kg}/\text{day}$ (^{70 kg adult} ~~adult male~~). Exposure by ingestion of NTA from dinnerware has been estimated to be 0.07 $\mu\text{g}/\text{kg}/\text{day}$ (^{70 kg adult} ~~adult male~~) for rinsed and towel-dried dishes.

SECTION 3

HUMAN EXPOSURE DURING MANUFACTURE

PRODUCTION TECHNOLOGY FOR TRISODIUM NITRILOTRIACETATE

Trisodium nitrilotriacetate, the sodium salt of NTA, is currently being produced in the United States by Monsanto Chemical Company at the Chocolate Bayou Plant near Alvin, Texas, and by the W. R. Grace Company at Nashua, New Hampshire. The Monsanto plant, which has a production capacity of 100 million pounds annually, is reported to be operating at one-half capacity (Centofanti, 1978). Monsanto apparently ships all of its product to Canada for use in detergents. The W. R. Grace plant is reported to have a production capacity of 40 million pounds per year, but is now operating at a reduced rate, approximately 50% of capacity (Huber, 1978a; 1978b). It operates 24 hr/day and 5 to 7 days/week, depending on demand (Amirsakis and Cullen, 1978). Most of the W. R. Grace Company product is shipped to Canada, and most of the remainder* is used industrially in the United States. According to information provided by a spokesman for W. R. Grace (Huber, 1978b), Canada currently consumes about 60 million pounds per year of trisodium nitrilotriacetate (i.e., the sum of shipments to

* Two divisions of W. R. Grace (in Sweden and in England) purchase "relatively modest" amounts (compared to the total NTA production of W. R. Grace) of trisodium nitrilotriacetate for use in detergents and specialty applications (Amirsakis, 1979).

Canada from Monsanto and W. R. Grace in the USA). Based on this information, the current production rate for the Grace plant can be estimated as 15 to 20 million pounds of NTA per year.

A summary of current market data is shown in Table 1.

TABLE 1. 1978 MARKET DATA FOR NTA

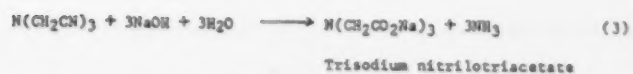
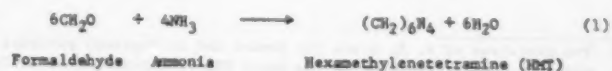
Manufacturer	Production ^{a/}		Distribution ^{a/}	
	Capacity	Actual	Export ^{b/}	U.S. consumption
Monsanto	100	50	50	0
W. R. Grace	40	20	10	10
Total	140	70	60	10

Source: Centofanti (1978); Huber (1978a; 1978b); Amirsakis and Cullen (1978).

^{a/} Quantities in million pounds.

^{b/} Canada.

The basic process chemistry for the W. R. Grace process according to Huber (1978b) is described by the following chemical reactions.

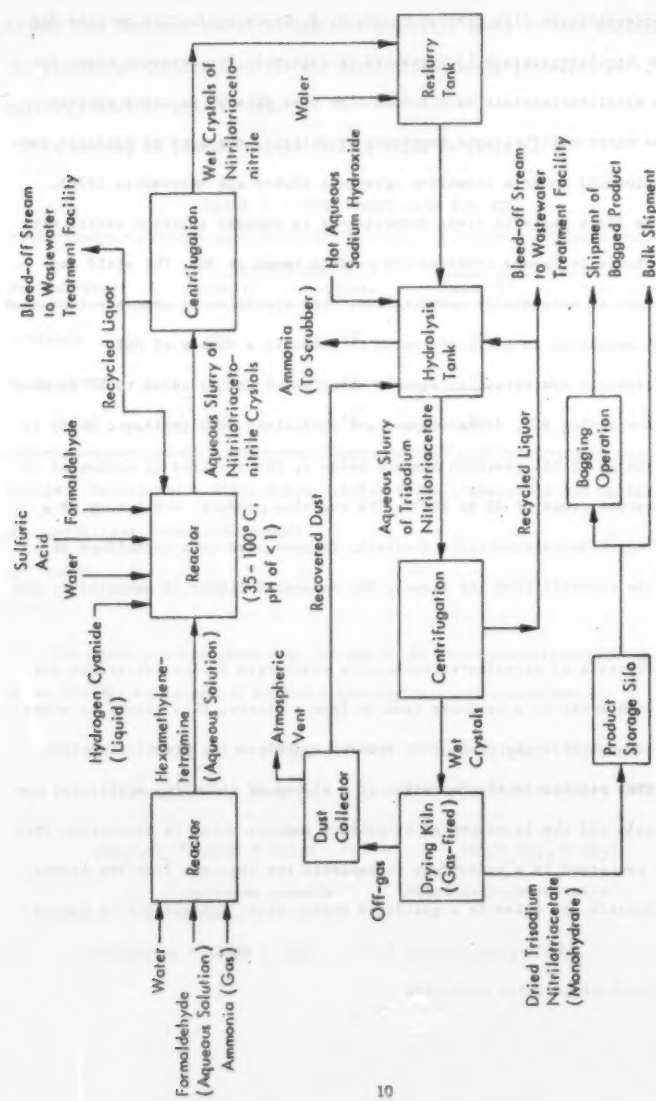


A representative flow diagram of the W. R. Grace production process for trisodium nitrilotriacetate is presented in Figure 1. The Monsanto plant for trisodium nitrilotriacetate manufacture also uses this W. R. Grace process (with some minor modifications involving principally the type of material conveying equipment) under a licensing agreement (Huber and Amisakis, 1978).

In the first reaction step, formaldehyde in aqueous solution reacts with gaseous ammonia to form a condensation product known as HMT. The yield for this reaction is essentially quantitative. This operation is commonly conducted as a batch operation in a closed system to maintain a supply of HMT.

In a typical operation, an aqueous solution of HMT is added to an aqueous solution containing HCN, formaldehyde, and sufficient acid (sulfuric acid) to maintain the pH of the reaction mixture below 1. The reaction is conducted in the temperature range of 35 to 100°C. The reaction product, consisting of a slurry of nitrilotriacetoneitrile crystals, is processed in a centrifuge to separate the crystals from the liquor. The separated liquor is recycled to the reactor.

Wet crystals of nitrilotriacetoneitrile discharged by the centrifuge are agitated with water in a reslurry tank to form a slurry. This slurry is added to a hot aqueous solution of caustic soda to hydrolyze the nitrile functions. This reaction results in the formation of a slurry of trisodium nitrilotriacetate crystals and the formation of by-product ammonia which is recovered. This slurry is processed in a centrifuge to separate the crystals from the liquor. The wet crystals are dried in a gas-fired drying kiln. Exhaust gas is passed



through a dust collector to an atmospheric vent; recovered dust is recycled to the hydrolysis tank.

Dried trisodium nitrilotriacetate, recovered as the monohydrate, $N(CH_2CO_2Na)_3 \cdot H_2O$, is transferred to a product storage silo. Product is removed from the silo and transferred to a bagging operation or to a bulk shipment station where the material is loaded into hopper bottom railroad cars.

As indicated in Table 2, the typical commercial product purity is greater than 99%. Quantitatively, the most significant impurities are inorganic salts, including sodium hydroxide and sodium carbonate. Also present are small quantities of iminodiacetic acid (IDA). The other impurities such as HCN and trace metals are present at low parts-per-million levels (Winters, 1977). In response

to a Midwest Research Institute (MRI) question, a formaldehyde analysis was performed ^{by Monsanto on a plant sample} which indicated that the product contained ^{at most} 2 ppm formaldehyde. ^{(i.e. filling that releases formaldehyde in acid will give a positive response).}

NTA is formulated into a detergent, it has little tendency to degrade. Under carton/shelf exposure conditions of moisture and air, NTA is completely stable. P&G Canada routinely monitors its NTA-containing detergents (a) as made, (b) in the warehouse, and (c) in the trade; no measurable degradation has been detected. NTA may be oxidized, but it takes a strong oxidizing agent--stronger than present components in detergent products using NTA (Winters, 1978b).

There are a number of U.S.-based companies (e.g., Olin Corporation, Geigy Chemical Corporation, Ethyl Corporation) which, although not presently producing NTA domestically, hold patents for its manufacture and could presumably enter the business if market trends warrant such action.

TABLE 2. IMPURITIES IN TRISODIUM NITRILOTRIACETATE

Impurity	Level
HCN	4 ± 2 ppm
NaOH	$0.3 \pm 0.1\%$
Na_2CO_3	$0.4 \pm 0.1\%$
Primary and secondary amines	$\sim 0.2\%$
Iminodiacetic acid (IDA)	$(0.2 \pm 0.05\%)$
Trace metals (partial)	
K	6 ppm
Zn	2 ppm
Cu	1 ppm
Fe	< 10 ppm
Pb	1-2 ppm
Formaldehyde	≤ 2 ppm

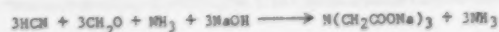
single batch analyses

Source: Winters (1977), except formaldehyde from Hopping (1978).

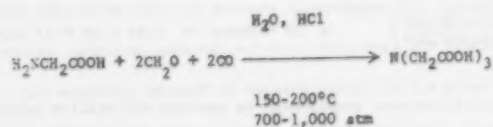
Olin Corporation holds U.S. Patent No. 3,578,709 (May 11, 1971) concerning "Preparation of Alkali Metal Salts of Nitrilotriacetic Acid" (Bishop and Jache, 1971). This method involves heating triethanolamine in the presence of a zinc oxide or cadmium oxide catalyst at 150 to 300°C with a mixture of sodium hydroxide and a minor proportion of potassium hydroxide. The reaction, where M is an alkali metal, is:



The Geigy Chemical Corporation holds U.S. Patent No. 3,415,978 (December 10, 1968) concerning "Process for the Production of Alkali Metal Salts of Nitrilo Triacetic Acid" (Gaunt, 1968). The process involves adding an aqueous, mineral-acid-stabilized, equimolar mixture of HCN and formaldehyde to an aqueous solution of an alkali metal hydroxide and ammonia. The reaction is:



The Ethyl Corporation holds U.S. Patent No. 3,470,245 (September 30, 1969) concerning "Preparation of Nitrilotriacetic Acid" (Jackisch, 1969). The NTA is prepared by the reaction of glycine with carbon monoxide and formaldehyde in the presence of aqueous hydrogen chloride. The chemical reaction is:



ESTIMATED NUMBER OF U.S. PRODUCTION WORKERS FOR NTA

In November 1978, the estimated annual production rates for NTA products were 30 million pounds for the Monsanto Chemical Company and 15 to 20 million pounds for the W. R. Grace Company.

Based on information provided by Huber (1978a), the operating manpower for the Grace NTA plant is estimated to be four workers per 8-hr shift or 12 men per 24-hr operating day. The manpower required for the current Monsanto operations as indicated by Metcalf (1978) is approximately 20 workers. Thus, the total U.S. plant labor force currently involved in production of NTA is estimated to be 32 workers.

The total number of plant workers required for levels of production larger than 50 million pounds annually can be estimated as follows. Peters and Timmerhaus (1968) have indicated that a "one-fourth factor" can be used to scale up labor requirements from one plant size to a larger plant size. This factor takes into account the fact that larger plant sizes require less than proportional labor forces because of economies of scale.

For a projected NTA production rate of 400 million pounds NTA per year, there would probably be two plants each with production rates of 200 million pounds per year. On this basis, the estimated number of workers required is:

$$2 \times \left(\frac{200,000,000}{50,000,000} \right)^{0.25} \times 20 \text{ workers} = 2.83 \times 20 = 57 \text{ workers}$$

Thus, the estimated manpower requirement to produce 400 million pounds per year is 57 workers per 24-hr operating day.

If annual production were increased to 1 billion pounds per year, there would probably be three or four plants whose individual total production rate would average 250 to 350 million pounds per year. Based on the above assumptions, the required labor force per 24-hr operating day is equal to:

$$4 \left(\frac{250,000,000}{50,000,000} \right)^{0.25} \times 20 = 120 \text{ workers, or}$$

$$3 \left(\frac{350,000,000}{50,000,000} \right)^{0.25} \times 20 = 98 \text{ workers.}$$

Thus, the projected labor force for the three production levels is as follows: 70 million pounds (current level) requires 32 workers; 400 million pounds would require 57 workers; and 1 billion pounds would require 98 to 120 workers.

ANALYSIS OF PROBABLE WORKER EXPOSURE TO NTA IN MANUFACTURING OPERATIONS

An analysis of the processing unit operations used in manufacturing NTA was presented in Figure 1.

The entire production process is automated and all workers, except those engaged in product packaging and loading activity, are provided with a remote control room where they spend much of their time in data monitoring and recording activity separated from the process operations. The automatic plant features include process sampling, process material weighing, and transfer and conveying equipment. Air monitors located at various points in the plant area trigger an alarm in the event of any process leaks of toxic material (e.g., HCN).

The first process step involves the reaction of formaldehyde with ammonia to form MHT. The risk of worker exposure in this step appears to be minimal since the reaction is carried out by remote control and the equipment is monitored for gas leaks. The MHT is discharged as an aqueous solution, thus minimizing the possibility of work area contamination with airborne dusts containing process chemicals.

The second reaction step and the subsequent centrifuging step are conducted in a closed system, primarily because of the involvement of highly toxic HCN. Therefore, the risk of worker exposure to reactants, HCN contaminants, or by-products in the operating area for these operations appears to be negligible with the exception of special ^{but controllable exposure} hazards which could be created by equipment failure (i.e., breakdown or rupture of equipment resulting in spills or leakage of chemicals to the working area).

The transfer of crystals of nitrilotriacetoneitrile from the centrifugation step to the reslurry step is also carried out by remote control, thus restricting worker contact. It appears that the degree of potential exposure in this area would probably be quite low because the crystals are wet and therefore unlikely to create any dust problems.

In the hydrolysis and centrifugation steps, all process operations are carried out in a liquid phase again by remote control. The separated crystals of trisodium nitrilotriacetate are wet and thus the prospects for generation of dust (i.e., skin or inhalation exposure to dusts) in this area appear to be remote. Ammonia formed as by-product during the hydrolysis reaction is recovered.

The wet crystals are dried to produce a powdered product. In the drying step, the off-gas containing fuel combustion products, water vapor, and some dust (sodium salt of NTA) is passed through a dust collector and then vented to the atmosphere. Dust recovered by the dust collector is transferred to the hydrolysis tank for reprocessing.

Dust losses of product are apt to occur to the work atmosphere of the drying kiln, the product packaging area, and the product bulk loading operations. Therefore, the risk of worker exposure via both skin contact and inhalation appears to be greatest for these operations.

In summary, the potential for exposure to NTA during the various steps in the manufacturing process is as follows:

<u>Manufacturing step</u>	<u>Potential for NTA exposure</u>
Formation of NMT	Minimal
Reaction of NMT with HCN	Minimal
Centrifugation and reslurry	Minimal
Hydrolysis and centrifugation	Minimal
Drying	Very large if no precautions employed
Packaging and bulk shipment	Very large if no precautions employed

Proper precautions which can significantly reduce the exposure risk include:

- Adequate ventilation and dust control equipment.
- Use of proper protective apparel by workers, e.g., gloves, impervious work clothing, and filter masks, or airline breathing masks.

The Monsanto and Grace companies both report that their plants observe these safety precautions.

In summary, since the production of NTA is highly automated and operated by remote control, production workers have a high exposure potential to only the trisodium salt of NTA--the final product--in the bagging and loading operations. The final product is of at least 99% purity; the contaminants are NaCl (4 ppm), sodium hydroxide (0.3%), sodium carbonate (0.4%), primary and secondary amines (0.2%), formaldehyde ($\leq 1 \text{ ppm}$), and trace metals (Table 2; Winters (1977)).

WORKER EXPOSURE DATA

Actual worker exposure data have been compiled at the Monsanto (Chocolate Bayou) facility (Hill et al., 1977). Urine samples were taken for analysis, and air in the breathing zone of each worker was monitored.

Two 24-hr urine samples were collected from each NTA plant worker. Each sample was collected over the 24-hr period approximately in the middle of the workweek. The two samples were taken at approximately 1-week intervals. NTA was not detected in the urine samples (by GC/MS) at or above the limit of detection, 0.5 mg/liter.

Monsanto (Hill et al., 1977) assumed that, since the "metabolism of NTA occurs with excretion of a significant portion (mean value 13%) of unchanged NTA in urine," urinary levels could be used to measure the exposure to NTA. The 13% mean value was reported by Buday and Arnold (1973) who administered 10 mg of NTA orally, in a single dose, to human volunteers; the dose level varied from 0.107 to 0.169 mg/kg. The percentage of NTA excreted unchanged by the subjects was $12.33 \pm 7.41\%$; thus, the probable variation is from 5 to 19%.

Based upon the 1% excretion level, and assuming that NTA concentrations in the urine were at the minimum detectable level, Monsanto calculated maximum

18 daily intakes which ranged from $< \frac{1.69}{4.05}$ to < 13.86 mg.

An important question is the validity of the 1% value for the excretion level; in the study, human volunteers received 10 mg orally at one time; however, the air analyses (described later) indicate that the workers were ordinarily exposed by inhalation to 0.1 to 0.5 mg during the entire course of an 8-hr work shift. The lower intake level and the different route of administration could result in substantially different excretion rates and quantities of NTA.* If so, there could be wide variation in the level of exposure which could be detected. For example, ^{even} if all of the NTA were ^{absorbed} ~~metabolized~~ at the lower intake level, the ~~X~~ urinalysis would be incapable of measuring the extent of exposure.

In these studies, toluene was used as a preservative for urine. Toluene is not ordinarily used for this purpose (Bio-Science Handbook, 1978) but was selected because no NTA-metal complexing problems would be encountered (NTA complexes with some of the metal-containing preservatives) and NTA is

* Consultations concerning this question were held with Dr. C. C. Lee, Deputy Director of the Pharmacology and Toxicology Department, Dr. Harry V. Ellis III, Senior Pharmacologist, and Dr. Betty L. Herndon, Associate Pharmacologist, all of MRI. The consensus of opinion is that, in the absence of additional data, it is not possible to assume that 1 mg oral doses and 0.1 mg inhalation doses would result in comparable quantities or rates of NTA excretion. The absorption mechanisms are markedly different and the metabolic patterns could be significantly different. Since most of the NTA is metabolized, these pharmacologists suggest that a better method of urinalysis to detect exposure might be based upon a major metabolite. — *As his/her metabolism occurs in the body. Thus, no metabolite is excreted.*

practically insoluble in toluene. Also, since polarographic analyses were to be performed, acidification of the urine was undesirable (Ward, 1979).

In the air analyses, full period breathing zone monitoring of each worker was performed during the 8-hr shift for which the 24-hr urine sample was collected. "Potential inhalation exposures"* ranged from 0.1 to 8.2 mg NTA per shift with a minimum quantitative level of 0.1 mg NTA per day. There were three distinct levels of NTA in the air samples. In the "normal" line area,** exposure levels of 0.1 to 0.5 mg NTA per day were usually found. The highest potential exposure was to the hopper-car loader with normal exposure periods of only 30 to 60 min/day. The hopper-car loader had an 8-hr average potential exposure of up to 10 mg NTA per workday. (This potential exposure assumes that the hopper-car loader does not wear a respirator; however, a respirator is required for this operation.) There was one intermediate level of exposure (maximum exposure potential of 5.7 mg/day) which occurred during a plant outage (caused by a rain storm), during which NTA had to be manually removed from carrier belts, and the resulting spills in this area were hosed down the drain.

As shown, calculations based upon the Monsanto data indicate that the worker with the highest potential in inhalation exposure is the hopper-car loader.

* "Potential inhalation exposures" were calculated by Monsanto (Hill et al., 1977) based on the time-weighted average concentration of NTA in the air the standard workday tidal volume. It was assumed that the worker had no respiratory protection and that no inhaled NTA was exhaled.

** Of the three areas in which NTA exposures were measured, the "normal" line area represents all areas other than the area where the hopper-car loader works (Ward, 1979).

Area	Potential exposure ^{a/} (mg NTA/shift)	Time-weighted average concentration ^{b/} (mg NTA/m ³)	Average concentration during shift ^{c/} (mg NTA/m ³)
Normal line area	0.1-0.5	0.01-0.05	0.01-0.05
Hopper-car loader	8.2	0.82	6.56
During plant outage	5.7	0.57	0.57

a/ From Hill et al. (1977).

b/ MRI calculations. Time-weighted average concentration (mg NTA/m³) equals potential exposure ÷ 10 m³ (standard workday tidal volume).

c/ MRI calculations. The actual exposure time for the hopper-car loader was reported to be 30 to 60 min (Hill et al., 1977) and for the purpose of this estimation was presumed to be 1 hr. The other exposure periods were 8 hr (Ward, 1979).

The relatively very high concentrations of NTA in the area of the hopper-car loader can also be estimated from other data as follows: Hill et al. (1977) reported that the respirator of the hopper-car loader contained 4.5 mg NTA on one occasion and 7.8 mg NTA on another. If the NTA in the respirator represents the amount collected during a single exposure period (1 hr), the average concentration of NTA in the air can be calculated by assuming that the amount of NTA in the respirator was equal to the amount of NTA in the air inhaled by the worker during the 1-hr exposure period (one-eighth of the standard workday tidal volume, 1.25 m³). Thus the calculated average NTA concentrations are:

$$\frac{4.5 \text{ mg}}{1.25 \text{ m}^3} = 3.6 \text{ mg/m}^3$$

$$\frac{7.8 \text{ mg}}{1.25 \text{ m}^3} = 6.2 \text{ mg/m}^3$$

These figures are in general agreement with the calculated level 6.56 mg/m³.

The following data concerning the exposure of MT₂ production workers to other products were provided by Monsanto (Metcalf, 1978b).

Ammonia - The American Conference of Governmental Industrial Hygienists (ACGIH) limit is 25 ppm (time-weighted average).

A series of area measurements in highest exposure potential zones using long-term detector tubes results in ambient concentrations generally below 10 ppm. Considering the limited exposure time of operators in such areas, worker exposures on an 8-hr basis have been calculated to be less than 1.0 ppm time-weighted average. A 10-fold variation in airborne concentrations versus worker time-weighted average exposure is not uncommon in processes having dynamic work patterns.

HCN - The ACGIH limit is 10 ppm (ceiling).

Utilizing long-term detector tubes specific for HCN, the environmental concentrations are for the most part less than the tube lower detection limit of 0.25 ppm. HCN is handled in completely contained systems where even minor leakage cannot be tolerated. Routine exposure to operators is nil.

Two continuous HCN monitors are located in the NTA unit to alert personnel of possible emergency situations. Both units are set to alarm at 6 ppm.

Formaldehyde - The ACGIH limit is 2 ppm (ceiling).

The exposure information on formaldehyde is more subjective. Formaldehyde, while quite irritating at high concentrations, can be easily recognized at airborne concentrations of 1.0 ppm and detected by experienced personnel at

somewhat lower levels. Monitoring surveys in formaldehyde handling areas using impinger collection followed by colorimetric analysis have substantiated these odor/effect properties.

While little objective monitoring data on formaldehyde exposure in the Monsanto process have been developed to date, the observations and judgment of the plant professionals indicate trace odors of formaldehyde being present in highest potential exposure areas.* Area monitoring is scheduled to confirm our assessment of worker exposures being less than the 2.0 ppm ceiling and certainly less than 0.5 ppm on a TWA basis.

* Mr. J. S. Metcalf, Manager, Product Acceptability, Detergents, and Phosphates Division, was asked about these areas on February 9, 1979, by Dr. Alfred F. Heiners. Mr. Metcalf said that sampling for formaldehyde was done at a variety of locations throughout the plant. Although he did not remember the exact layout of the plant, he knew that the sampling was done in a number of areas where one would reasonably expect to detect formaldehyde, such as in areas where the reactor was opened and closed.

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SECTION 4

HUMAN EXPOSURE DURING DETERGENT FORMULATION

DESCRIPTION OF DETERGENT FORMULATION PROCESS

- The method currently being used for the commercial formulation of ~~granular~~ ^{primarily} basic detergents is a batch process. In the making of powdered detergents, raw ingredients, stored in tanks or bins, are pumped or conveyed through a ~~closed system to mixers, and blended into a slurry.~~ ^{reducers and then} The slurry is sprayed from the mixer into drying towers to achieve the desired granulation size and moisture content. Additional raw materials can also be added after the drying process. The finished powder is then conveyed to production lines where it is automatically put into cartons and packed for shipping. The industry-wide level of NTA used in powdered detergent ~~is currently 15% in Canada, where a nationwide limit of 2.2% phosphorus is in effect.~~ ^{averages}
- 22 Powdered cleansers are also formulated by ^{primarily} a batch process. These products are dry mixes which contain small quantities of detergent; ~~they would probably~~
- 23 ~~contain less than 1% NTA if NTA were used in detergents. The filling and packing~~
- 24 ~~in production lines for cleansers are major sources of dust contamination, particularly in the can filling operation.~~ ^{can be}
- 25 Liquid laundry detergents are also ^{primarily a process}
- 26 formulated by the batch in a closed system. The major steps in this operation

include pumping the raw materials from storage tanks into mixers. After mixing, the liquid is bottled and packed by automatic equipment.

AREAS IN EXPOSURE IN DETERGENT PLANTS

The workplace atmosphere can become contaminated with detergent dust containing NTA from leaks in the product lines, spills caused by a malfunction in equipment, equipment cleanup operations, and from operations which require manual handling of bags of NTA. The filling and packing production lines can become high dust areas, particularly when powder is spilled as a result of machine jams and product changeovers.

NUMBER OF WORKERS EXPOSED

The total number of production workers that would be directly exposed to NTA from the manufacturing of detergents in the United States is estimated by NIOSH to be 2,500. This figure is the estimated number of workers currently exposed to detergent dust in the workplace. The use of NTA would not change the number of workers required to produce detergents at the present market level.

The total number of production workers in the soap and detergent industry in 1976 was 23,400 (U.S. Department of Labor, 1976). Procter and Gamble has "somewhat over 1,000 workers" involved in the manufacture of detergents in the United States, and their estimate of current industry-wide exposure is double that figure, or approximately 2,000 (Winters, 1978^a).

About 70% (or roughly 700) of the Procter and Gamble workers are involved in the manufacture of granular laundry detergents. Furthermore, only about one-half of these workers enter the dustiest areas of detergent manufacture which

are the areas where the detergents are moved, boxed, or packaged (Hopping, 1979).

EXPOSURE LEVELS

30 Occupational exposure to airborne detergent dust (measured as total dust) in detergent formulation has been measured (Winters, ^{1978b} ~~1978~~). The total dust level, as a time-weighted average, was 1.38 $\mu\text{g}/\text{liter}$ (1.38 mg/m^3). This figure is an average proportioned by the time spent in the three dustiest areas associated with detergent manufacture. The range of concentrations for these three areas (in micrograms per liter) are: 2.33, 1.11, and 0.67 (Hopping, 1978). It was assumed that a worker spends one-third of his time in each area.

On the basis of these dust levels, the estimated NTA inhalation exposure was calculated (Winters, ^{1978b} ~~1978~~) to be:

Person exposed	Exposure ($\mu\text{g Na}_3\text{NTA}/\text{kg}/\text{day}$)	
	Typical	Extreme
Adult male (70 kg)	< 4.8	48.3
Adult female (54 kg)	< 3.6	35.7

* These three areas of higher dust concentrations are those in which the detergent is moved, boxed, or packaged. The average of these three concentration levels (1.38 $\mu\text{g}/\text{liter}$) provides a time-weighted average concentration assuming that a worker spends an equal time in each area. Procter and Gamble believes that this assumption is reasonable; the areas are in close proximity and workers do actually spend approximately one-third of their time in each area (Hopping, 1979).

The calculations were made as follows:

Breathing rate

Adult male (70 kg), light work $\frac{17.1 \text{ breaths}}{\text{min}} \times 1.673 \frac{\text{l}}{\text{breath}} = 28.6 \text{ l/min}$
(tidal volume) (Biology Data Book, 1974).

Adult female (54 kg), light work $\frac{19 \text{ breaths}}{\text{min}} \times 0.860 \frac{\text{l}}{\text{breath}} = 16.3 \text{ l/min}$
(tidal volume) (Biology Data Book, 1974).

Exposure time - 8 hr/day x 5 days/week = 40 hr/week.

Per day, weekly basis - 40 hr/week x 1/7 day/week = 5.71 hr/day.

Note: The 5.71 hr/day exposure time is on a weekly basis to be comparable to the other estimated exposure.

Estimated exposure

Adult male $\frac{1.38 \text{ ug/l} \times 0.25^* \times 28.6 \text{ l/min} \times 60 \text{ min/hr} \times 5.71 \text{ hr/day}}{70 \text{ kg}} = 48.3$
 ug/kg/day.

Adult female $\frac{1.38 \text{ ug/l} \times 0.25^* \times 16.3 \text{ l/min} \times 60 \text{ min/hr} \times 5.71 \text{ hr/day}}{54 \text{ kg}} =$
35.7 ug/kg/day.

Note: This exposure estimate assumes that all the measured dust is detergent, that all of the dust is respirable, that all of the inhaled dust remains in the body, and that the 7-day breathing rate is that corresponding to light work. Industry sources believe that at most no more than 40% of the dust is respirable, and that in reality < 10% would be respirable.

* A 25% content of NTA in the detergent is assumed. This would represent maximum concentrations.

In our opinion, the Procter and Gamble calculations provide a reasonable estimate of average occupational exposure to NTA in the dustiest areas of detergent manufacture. The calculations were made for the Hamilton, Ohio, plant for which an average dust level of 1.38 mg/liter was determined. Recent data (Hopping, 1979) indicate that time-weighted average dust levels in these areas are less than 1 mg/liter. Also, a 29% content of NTA in the detergent is used in the calculations; actual NTA content would probably not reach this concentration. Furthermore, in all of the studies, total dust levels were measured, and some of this dust is known to be material other than detergent (Hopping, 1979).

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SECTION 5

CONSUMER EXPOSURE TO DETERGENTS

The total consumer exposure to detergents includes exposure from:

- . Inhalation of detergent dust in home uses.
- . Percutaneous absorption from contact with wash water including laundry, dishwashing, and other operations such as mopping floors and general cleaning.
- . Percutaneous absorption from skin contact with detergent when measuring detergent, handling the box of detergent, or cleaning a spill of detergent.
- . Percutaneous absorption from skin contact with residues in clothes.
- . Ingestion of residues left on dishes and utensils.

NUMBER OF CONSUMERS EXPOSED

A summary of the number of consumers potentially exposed to NTA while using selected detergents is presented in Table 3.

Laundering Operations

The primary exposure from the use of NTA laundry detergents would occur while performing laundering operations. (Subsequent exposures may occur from residues on clothes.) The number of people in the United States that could be exposed to NTA while doing laundry has been estimated to be 174 million, or 81% of the total population (MEI estimate). This figure is based on the

TABLE 3. NUMBER OF CONSUMERS POTENTIALLY EXPOSED TO NVA WHILE USING SELECTED DETERGENTS

Product	Use	Route(s) of exposure	Potential No. persons exposed per household ^{a/}		Remarks
			Total ^{b/}	Most often exposed ^{b/}	
Powdered laundry detergent	Automatic clothes washers	Inhalation	174×10^6	76×10^6	Based on total number of households (industry data)
Powdered laundry detergent	General cleaning and hand laundry	Percutaneous and inhalation	174×10^6	76×10^6	All persons at some time may contact detergent with wet hands, put hands into wash water, or do general cleaning
Powdered laundry detergent	Dishwashing by hand	Percutaneous and inhalation	5×10^6	2×10^6	
Powdered laundry detergent	Automatic dishwashing	Inhalation	33×10^6	14×10^6	Based on estimated 14 million households with automatic dishwashers
Light duty detergents (liquid)	Hand dishwashing	Percutaneous	144×10^6	60×10^6	Based on number of households who use liquid detergents; assume no exposure via inhalation because most light duty detergents are liquid
Light duty detergents (liquid)	General cleaning and hand laundry	Percutaneous	174×10^6	76×10^6	Based on total number of households

^{a/} Assuming that everyone in household over 10 years of age uses the detergent product at some time.

^{b/} Assuming that one person per household uses the detergent product.

estimate that all members of a household over 10 years of age are likely to operate a washing machine at some time (AHAM, 1978). The Statistical Abstracts compiled by the U.S. Department of Commerce (1977) show the number of households (72.8 million), the average size of the household (2.89 persons), the percentage of the population over 10 years of age (calculated to be 83%), and the total population as of 1976 (213 million).

However, an industry source estimates that there are only 76 million persons who actually do laundry. This figure is based on the number of households (76 million) and assumes that one person per household does the laundry.* The MRI estimate represents the total number of persons exposed, while the industry estimate represents the number of persons who are most often exposed. (One person per household probably does laundry more often than other household members.)

Dishwashing Operations

In addition to laundry exposure, consumers may be similarly exposed when laundry detergents are used for dishwashing. An industry source estimates that 2 million households (persons) in the United States use laundry detergents for dishwashing by hand. Assuming that everyone in the household over 10 years of age washes dishes at sometime, a maximum of 5 million persons would be exposed.

Currently, NTA is not used in any dishwashing detergents in the United States or Canada (Winters, 1976^{1978a}); however, the potential for the use does exist.

* Note that the estimates made by industry and by MRI pertaining to the number of households in the United States and the average size of a household are not identical; however, the difference is not significant.

Automatic Dishwashers--

38 If NTA were used as an automatic dishwashing detergent, the primary exposure would occur while pouring and handling the detergent prior to actual operations. (Subsequent exposure may occur from residues on dishes.) An estimated 33 million persons would be exposed to NTA while using an automatic dishwasher. This figure is based on an estimated 14 million households in the United States with automatic dishwashers; an average of 2.83 persons per household (data from an industry source) ~~the same source (1978)~~, with an assumption that everyone in the household over 10 years of age will use the dishwasher at some time (MRI estimate). However, the same industry source (1978) estimates that only one person per household uses the dishwasher; consequently, an estimated 14 million persons would be exposed. The MRI estimate represents the total number of persons exposed, while the industry estimate represents the number of persons who are most often exposed. (One person per household probably uses an automatic dishwasher more often than other household members.)

Hand Dishwashing--

40 If NTA were ~~used~~^{used} in a light duty liquid detergent for dishes, an estimated 174 million persons would be exposed via percutaneous absorption. This estimate is based on an estimated 76 million households doing dishes by hand and 2.83 persons being in each household (industry source, 1978), and the assumption that everyone in the household over 10 years of age may wash dishes by hand at some time (MRI estimate). However, 76 million persons would be exposed if one assumed that only one person per household does dishes (industry

source, 1978). Both of these estimates include households with automatic dishwashers, since even persons with automatic dishwashers ^{could} wash dishes by hand at some time.

A2 Of the estimated 76 million households ~~persons~~ exposed to NTA by hand dishwashing, only 60 million would be exposed on a regular basis to NTA from a light duty detergent. This estimate is based on the following information (industry source):

- Number of persons doing dishes
 76×10^6 - assume 1 person/household does dishes
- Number of households ~~(persons)~~ doing dishes by hand on a regular basis
 62×10^6 - assume 1 person/household does dishes
- Number of households ~~(persons)~~ using automatic dishwashers
 Assume 14×10^6 ($76 \times 10^6 - 62 \times 10^6$) - assume 1 person/household does dishes
- Number of households ~~(persons)~~ using liquid dishwashing detergents
 60×10^6 - assume 1 person/household does dishes
- Number of persons using laundry detergents for doing dishes by hand
 Assume 2×10^6 ($62 \times 10^6 - 60 \times 10^6$) - assume 1 person/household does dishes

Currently, most light duty detergents are liquid, so that the potential for exposure via inhalation would be minimal. However, the potential for dermal exposure would remain.

Residues in Clothing

Exposure to NTA also occurs from residues in clothes following laundering. Although this exposure is less than when doing laundry, virtually everyone in the United States would be exposed via this route.

Residues on Dinnerware

43 Exposure to NTA would also occur from residues on dinnerware following dish washing with an NTA laundry detergent, automatic dishwashing detergent, or light duty detergent if NTA were ^{used} ~~cleared for use~~ in these products. An estimated 5.8 million persons would be exposed (2.89 persons per household x 2 million) following hand washing with laundry detergent; 40 million persons (2.89 persons per household x 14 million) exposed following dishwashing dishwashing in an automatic dishwasher; and 213 million persons (U.S. residential population) exposed following hand washing of dishes with a light duty detergent. (Note: Even those households with automatic dishwashers wash dishes and utensils by hand at some time.)

Hand Washing, Mopping, and General Cleaning

Currently, powdered laundry detergents are used for some general cleaning, as well as for hand washing of clothes. In addition, the use of NTA in cleansers and light duty detergents used for hand washing, mopping, and general cleaning may be considered in the future (industry source, 1978).

Use of detergents containing NTA, intended for general cleaning, would result in the exposure of 174 million persons (NRI estimate). This figure was calculated as before, based on the assumption that everyone in a household over 10 years of age might do hand washing of clothes or general cleaning at some time.

EXTENT OF EXPOSURE

Consumer exposure to NTA if used in detergent products in the United States is most likely to occur during actual use of the product; significantly less exposure is expected from contact with any residues remaining on those items washed in the detergent.

Exposure by Inhalation

Consumer inhalation exposure to NTA can be expected during use of powdered laundry detergents for washing clothes (and general cleaning) and during use of powdered dishwashing detergent products.

Home Laundry Operations--

The airborne concentrations of detergent expected around a laundry site have been determined by Procter and Gamble Corporation (Hendricks, 1970) and Colgate-Palmolive (Hudson, 1978). From these data, the expected airborne NTA concentrations can be calculated if NTA were used in similar formulations of powdered laundry detergents.

From in-home dust collection studies conducted during typical consumer use (Hendricks, 1970), it has been estimated that the average dust exposure for an average female is 0.27 $\mu\text{g}/\text{cup}$ of detergent product used. This figure ~~is based on a female inhalation rate of 16.3 liters/min and the double-pour method which is the most common method of dispensing powdered detergent. (The double-pour method involves pouring the product from the carton into a measuring aid and then into the washing machine.) The double-pour method generates more dust than any other method or use of a laundry product in the home (Hendricks, 1970). Consumer usage of laundry detergent was calculated; the~~ *is based on a female inhalation rate of 16.3 liters/min and the double-pour method which is the most common method of dispensing powdered detergent. (The double-pour method involves pouring the product from the carton into a measuring aid and then into the washing machine.) The double-pour method generates more dust than any other method or use of a laundry product in the home (Hendricks, 1970). Consumer usage of laundry detergent was calculated; the*

average amount used per week is 7.8 cups, and at the upper 95th percentile the figure is 22.5 cups/week. The industry-wide average concentration of NTA in Canadian powdered laundry detergents is approximately 15% by weight; the maximum amount that is being used in Canada is 25%.

For calculations of consumer exposure, NTA is assumed to be homogeneously distributed throughout all size granules; however, NTA may be preferentially ~~associated with~~ ^{associated with} the larger or smaller sized particles. Studies to determine the respirability of detergent dust were not available; consequently, in the estimated exposure to NTA in powdered detergents, exposure to both the respirable and nonrespirable fractions of detergent dust is assumed.

The following is the calculated consumer exposure to NTA via inhalation (Winters, 1978) ^{MRI calculations} expressed as micrograms of Na_2NTA per kilogram per day.

User	Typical	Extreme
Female adult (54 kg)	0.001	0.004
Male adult (70 kg)	0.002	0.005
Child (10 kg)	0.006	0.020

These data were calculated based on the following formula:

$$\frac{(\text{detergent dust/cup})(\% \text{ NTA in detergent})(\text{weekly detergent use}) \times (\text{week/day})}{(\text{body weight})}$$

The data used in the calculations are presented below:

- 48 - 0.27 μg detergent dust exposure per cup for an adult female, measured in home use, ~~based on an average inhalation rate of 16.3 liters/min~~ (Hendricks, 1970).
 simulated

Neglect. Is correct as written

49 - 0.47 μg detergent dust exposure per cup for an adult male, based on ^{simulated} home ~~source~~ by Hendricks (1970) and an average inhalation rate of 28.6 liters/min (Biology Data Book, 1974).

50 - 0.24 μg ^{simulated} detergent dust exposure per cup for a 10-year-old child, based on ~~home source~~ by Hendricks (1970) and an average inhalation rate of 14.4 liters/min (Chemical Rubber Company, 1969).

- % of NTA in dust--23% - assumes 23% NTA in detergent with even distribution.

- detergent use--7.8 cups/week - median (Hendricks, 1970); and
--22.5 cups/week - 95th percentile (Hendricks, 1970).

Note: Includes other uses such as presoaking, floor washing, etc.

- median (typical) detergent use - the calculations were made as follows:

$$\text{Adult female } \frac{0.27 \mu\text{g/cup} \times 0.25 \times 7.8 \text{ cups/week} \times 1/7 \text{ day/week}}{54 \text{ kg}} = 0.001$$

$\mu\text{g/kg/day}$

$$\text{Adult male } \frac{0.47 \mu\text{g/cup} \times 0.25 \times 7.8 \text{ cups/week} \times 1/7 \text{ day/week}}{70 \text{ kg}} = 0.002$$

$\mu\text{g/kg/day}$

$$\text{Child } \frac{0.24 \mu\text{g/cup} \times 0.25 \times 7.8 \text{ cups/week} \times 1/7 \text{ day/week}}{10 \text{ kg}} = 0.006$$

$\mu\text{g/kg/day}$

- 95th percentile (extreme) detergent use:

$$\text{Adult female } \frac{0.27 \mu\text{g/cup} \times 0.25 \times 22.5 \text{ cups/week} \times 1/7 \text{ day/week}}{54 \text{ kg}} =$$

0.004 $\mu\text{g/kg/day}$

$$\text{Adult male } \frac{0.47 \mu\text{g/cup} \times 0.25 \times 22.5 \text{ cups/week} \times 1/7 \text{ day/week}}{70 \text{ kg}} =$$

0.005 $\mu\text{g/kg/day}$

$$\text{Child } \frac{0.24 \mu\text{g/cup} \times 0.25 \times 22.5 \text{ cups/week} \times 1/7 \text{ day/week}}{10 \text{ kg}} = 0.02 \mu\text{g/kg/day}$$

Note: These exposure estimates assume that all of the measured detergent dust is inhaled, that all of the detergent dust is respirable, and that all of the inhaled dust remains in the body. This is not expected in actual practice.

The Colgate-Palmolive Company developed a test in 1970 to measure the amount of dust created from the use of several of its products. The test was designed to simulate the use of automatic washing machines. The actual test consisted of four people standing around a bucket 16 in. in diameter and 33 in. above the floor to simulate a washing machine. Each person poured powdered laundry detergent from a 49-oz box into a cup and the cup was emptied into the bucket. This was repeated until the boxes were empty. An air sampler was situated in an area which would be occupied by a fifth person around the bucket. The sampling was performed during the pouring of the detergents and for various time intervals after the pouring was complete (Hudson, 1978). The results of this study are presented in Table 4.

TABLE 4. DUST LEVELS FROM POWDERED DETERGENTS

Product No.	Total pouring time for 49 oz (min)	Total sampling time (min)	Total amount of dust collected ($\mu\text{g}/\text{m}^3$ of air)	Calculated amount of dust created by 1-1/4 cup over the sampling period ($\mu\text{g}/\text{m}^3$)
1	2	50	1,400	93
2	2	100	2,000	133
3	2	124	300	20
4	2	126	300	20
5	2	200	800	53

Source: Hudson (1978).

Ninety-five percent of detergent dust settles in 100 sec, virtually all detergent dust settles within 2 min (Hendricks, 1970). This information is based on a study using a laser dust detection device developed for this study.

51 Assuming the breathing rates used in the Procter and Gamble study and an average breathing time of $\frac{0.11}{2}$ min, the extent of exposure to the levels generated in the Colgate tests were estimated (Table 3).

TABLE 3. INHALATION EXPOSURE TO NTA CONTAINING POWDERED DETERGENT PER 1.25 CUP USE

Detergent product No.	For adult female ^{a/} NTA (ug/kg)	For adult male ^{a/} NTA (ug/kg)
1	0.014 0.001	0.019 0.001
2	0.020 0.001	0.027 0.002
3	0.003 0.0002	0.004 0.0003
4	0.003 0.0002	0.004 0.0003
5	0.008 0.0006	0.011 0.0008

Source: MRI calculations.

^{a/} Calculated as follows: breathing rate (16.3 liters/min, female; 28.6 liters/min, male) x exposure time $\frac{0.11}{2}$ min x dust concentration, ug/liter (Table 3-1) x $1 \text{ m}^3/1,000 \text{ liters}$ x maximum NTA content of detergent (0.23) ÷ average body weight (54 kg, female; 70 kg male) = estimate.

These values, which utilize dust concentrations determined by the Colgate-Palmolive Company, are within the range of exposures calculated in the Procter and Gamble study.

Automatic Dishwashing Operations--

The potential inhalation exposure to NTA associated with automatic dishwasher detergent use has not been studied. However, inhalation exposure from its use in an automatic dishwasher detergent is assumed to be similar to exposure estimated for laundry detergent (NRI estimate). On a per ^{USE} basis (daily consumer use is estimated to be ^{0.16} cup/day maximum; ^{Industry} the detergent dust exposure would be ^{0.043 (0.27 x 0.16)} μg for an adult female, ^{0.075 (0.47 x 0.16)} μg for an adult male, and ^{0.040 (0.25 x 0.16)} μg for a child, resulting in potential dust exposures of 0.0003, 0.0003, and 0.001 $\mu\text{g}/\text{kg}/\text{day}$, respectively. These data were based on the following formula:

$$\frac{(\text{detergent dust exposure}/\text{USE})(\% \text{ NTA in detergent})}{(\text{body weight})}$$

Exposure by Percutaneous Absorption

Percutaneous exposure can result from washing dishes, hand laundry, and general cleaning with a detergent containing NTA, contact with laundry machine washwater, or by wearing clothes which have been washed in a detergent containing NTA.

Hand Laundry and Dishwashing--

The following calculation summarizes exposure to NTA if it were added to laundry detergent or light duty detergent (liquid or powdered) and used to do 53 dishes or laundry by hand (Winters, 1978).

- calculation

$$\frac{(24 \text{ hr absorption}) \times (\text{skin area}) \times (\text{exposure time})}{(\text{body weight})}$$

data

24-hr absorption $0.25 \mu\text{g}/\text{cm}^2/\text{day}$ --highest measured for animal skin exposed for 24 hr to a solution of NTA and linear alkylbenzene sulfonate (LAS), each present 0.2% (wt/wt).^a

Notes: A typical product use for doing dishes or laundry by hand would be 0.2 to 0.3% (wt/vol) and the typical NTA concentration in the wash water for doing dishes (and laundry) by hand is 0.073% (0.73 g/liter). This concentration is about two times the concentration used in automatic laundry machines (Hopping, 1978).^a assuming a 2.5% level of NTA (a product (W. A. H. 1978)).

exposure time--1 hr/day--95th percentile, is 3.85 washes/day at about 13 min/wash; 0.5 hr/day--median, is about 2 washes/day at about 15 min/wash. (Hendricks, 1978).

$$1 \text{ hr/day exposure } \frac{0.25 \mu\text{g}/\text{cm}^2/\text{day} \times 1.680 \text{ cm}^2 \times 1 \text{ hr}/74 \text{ hr}}{70 \text{ kg}} = 0.25 \mu\text{g}/\text{kg}/\text{day}$$

$$0.5 \text{ hr/day exposure } \frac{0.25 \mu\text{g}/\text{cm}^2/\text{day} \times 1.680 \text{ cm}^2 \times 0.5 \text{ hr}/74 \text{ hr}}{70 \text{ kg}} = 0.13 \mu\text{g}/\text{kg}/\text{day}$$

Notes: Absorption flux used was measured at an NTA concentration much higher than which would occur in actual practice. The calculations also assume that absorption for human skin is the same as that for the animal skin.

^a A study was conducted in 1974 (Hopping, 1979) to determine the skin absorption potential of NTA. The experiment consisted of a single application of carbon-14 labeled NTA and LAS (each present at 0.2%) to the shaved skin of two rats. The animals were restrained for 72 hr and the urine and feces collected. The results showed a 72-hr absorption of $0.25 \mu\text{g}/\text{cm}^2$ for NTA.

Rat skin does not provide a simulation of human skin and is not commonly used for this purpose. Shaved rat skin generally permits greater penetration of chemicals than occurs through human skin so that the absorption rate is probably greater than that which would occur through human skin under normal conditions. Additional tests should be performed on other animal skin models before an approximation of human skin absorption can be assumed (Hendrickson, 1979).

a more precise

however, the values given here represent an upper limit for the ranges given above.

No data have been found concerning the exposure which could occur if concentrated solutions of detergent containing NTA came in contact with the skin. Similarly, skin absorption from contact with NTA products (laundry or dishwashing) in the powdered form has not been studied. The number of people exposed in this manner would be very large (all persons who handle boxes of detergents), but the contact time would probably be short compared to contact with dishwater.

(Most people would rinse their hands shortly after contact with powdered detergent.) The percutaneous data ^{provided} ~~obtained~~ by Procter and Gamble ^(Winters 1978) ~~44996~~ indicate

that an adult individual would be exposed to only 0.13 to 0.25 μg of NTA per day because of exposure to dishwater containing a concentration of 0.2% (wt/vol) (3.0 g/liter) NTA.

However, exposure of the dishwasher or launderer to detergent adhering to the container (or other sources of contact with the powder, such as spills) possibly results in a situation where a fairly highly concentrated solution of the detergent would be in contact with the skin (of the hands, particularly). No data are available to predict the percutaneous absorption rate of higher concentrations of NTA; but, because of the substantially greater quantity of NTA in contact with the skin, the rate might be significantly greater than 0.25 $\mu\text{g}/\text{cm}^2/\text{day}$, although the contact time would be short.

Laundry Machine Operations--

63 The NTA concentration expected in laundry machine washwater is 0.36 ^{g/liter} ~~wt~~ (0.036% wt/vol). This figure was calculated from the following data

64 (Winters, 1978; Hopping, 1978a).

- 1.25 cups detergent
- 77 g of detergent per cup
- 25% NTA
- 17.5 gal. wash solution volume

Contact with laundry machine washwater does not occur frequently, and when contact occurs it is usually of short duration. (Most people would rinse their hands following such contact.)

Residue in Clothes--

The extent of consumer exposure to NTA in clothes has been estimated by ^{b) Hopping, 1978 b) Hopping, 1978} Procter and Gamble (Winters, 1978) to be:

- calculation

$$\frac{(\text{conc. on fabric}) \times (\text{skin area exposed to fabric}) \times (\text{absorption efficiency})}{\text{body weight}}$$

⁶⁶ The following data were used:

- concentration on fabric $0.01 \mu\text{g}/\text{cm}^2$. Measured value for fabric laundered in NTA detergent.
- skin area exposed, assume complete coverage 24 hr/day: adult, $1.6 \times 10^4 \text{ cm}^2$ (70 kg); child, $5.5 \times 10^3 \text{ cm}^2$ (20 kg)
- absorption efficiency, ^{0.4%} highest measured for animal skin exposed for 74 hr to a solution of NTA and LAS, each present at 0.2% (wt/vol). The average NTA concentration in automatic laundry machine washwater is 0.036% (wt/vol), assuming 25% NTA in the detergent.

Note: A typical product use would be about 0.12% (wt/vol) of powdered laundry detergent.

61 - estimated exposure:

	$0.01 \mu\text{g}/\text{cm}^2 \times 1.6 \times 10^4 \text{ cm}^2/\text{day} \times \frac{0.008}{0.008}$	0.018
Adult	$\frac{70 \text{ kg}}{70 \text{ kg}} \times \frac{0.008}{0.008}$	$0.018 \mu\text{g}/\text{kg}/\text{day}$
Child	$\frac{20 \text{ kg}}{20 \text{ kg}} \times \frac{0.008}{0.008}$	$0.022 \mu\text{g}/\text{kg}/\text{day}$

Note: Not all body skin area is covered with clothes.

Exposure by Ingestion

This section describes potential exposure to NTA via ingestion if NTA were formulated into dishwashing detergents. ~~NTA is not currently used in the United States or Canadian dishwashing detergents in either automatic dishwashing formulations or in light duty detergents (those intended for hand dishwashing). In the event that NTA is used in the United States in detergent formulations, it is unlikely that NTA would be used in automatic dishwashing detergents in the near future (MRI estimate).~~ ^{To the best of our knowledge,}

Residues Resulting From Hand Washing of Dishes--

One percent of households (62×10^6) doing dishes by hand do not rinse their dishes (industry source, 1978). The following calculations summarize NTA exposure from residue on dinnerware resulting from washing dishes by hand and applies to both rinsed and nonrinsed dishes.

71 - calculation (Winters, 1978 b).

$$\frac{(\text{deposition on dinnerware}) \times (\text{area of dinnerware use}) \times (\% \text{ of area in contact with food})}{(\text{body weight})}$$

- data

Deposition on dinnerware $0.45 \mu\text{g}/\text{cm}^2$ --measured by chemical analysis for 25% NTA laundry product used at 0.2% (wt/vol) for dishwashing (rinsing and towel drying substantially reduces this amount); daily dinnerware area $4,300 \text{ cm}^2/\text{person}$; percentage of dinnerware area in contact with food 50% (or $\frac{4,300}{2150} \text{ cm}^2$).

- estimated exposure

$$\text{No rinse/drain dry--Adult } \frac{0.45 \mu\text{g}/\text{cm}^2 \times 4,300 \text{ cm}^2 \times 0.50}{70 \text{ kg}} = 13.8 \mu\text{g}/\text{kg}/\text{day}$$

$$\text{--Child } \frac{0.45 \mu\text{g}/\text{cm}^2 \times 4,300 \text{ cm}^2 \times 0.50}{10 \text{ kg}} = 96.8 \mu\text{g}/\text{kg}/\text{day}$$

Rinse/towel dry--

$$\text{Adult } \frac{0.45 \mu\text{g}/\text{cm}^2 \times 4,300 \text{ cm}^2 \times 0.50 \times 0.05 \times 0.10}{70 \text{ kg}} = 0.07 \mu\text{g}/\text{kg}/\text{day}$$

$$\text{Child } \frac{0.45 \mu\text{g}/\text{cm}^2 \times 4,300 \text{ cm}^2 \times 0.50 \times 0.05 \times 0.10}{10 \text{ kg}} = 0.48 \mu\text{g}/\text{kg}/\text{day}$$

Note: Rinsing dilutes concentration of adhering solution by 1/20; hence, 0.05 in equation. Towel drying removes 90% of adhering solution; hence, 0.1 in equation.

- hand dishwashers that do not rinse: One percent of the 62×10^6 households which do dishes by hand do not rinse; this equals 62×10^4 households doing dishes and not rinsing ($0.01 \times 62 \times 10^6$). Total persons affected, 1.8×10^6 (62×10^4 households $\times$ 2.83 persons/household).
- hand dishwashers who do rinse, followed by towel or drain dry: 99% of hand dishwashers; 61×10^6 households ($0.99 \times 62 \times 10^6$) do dishes by hand, rinse, and towel dry; total persons affected, 173×10^6 (61×10^6 households $\times$ 2.83 persons/household).

73 Residue Resulting From Use of an Automatic Dishwasher--

The concentration of NTA in the wash water of an automatic dishwasher would be present in the same concentrations as estimated for hand washing of dishes (MRI estimate) with an NTA laundry product, i.e., 0.05% or 0.5 g/liter (0.2% product with 25% NTA).

The estimated exposure to NTA from residue on dinnerware following washing in an automatic dishwasher for an adult is estimated to be between $13.8 \mu\text{g}/\text{kg}/\text{day}$ (the estimated exposure when hand washed dishes are not rinsed) and $0.07 \mu\text{g}/\text{kg}/\text{day}$ (exposure when hand washed dishes are rinsed and towel dried) (MRI estimate).

For a child the upper and lower limits would be 96.8 and $0.48 \mu\text{g}/\text{kg}/\text{day}$. These exposure estimates are not likely high, since the hot water rinses of an automatic dishwasher cycle could lead to less deposition on dinnerware than hand wash and rinse.

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EPA-560/11-79-008

CHEMICAL TECHNOLOGY AND ECONOMICS IN
ENVIRONMENTAL PERSPECTIVETask IV - Potential Worker and Consumer Exposure
to Nitritotriacetic Acid (NTA) in DetergentsFINAL REPORT
June 1979

Prepared under

Contract No. 68-01-3896

For

U.S. Environmental Protection Agency
Office of Toxic Substances
401 M Street, S.W.
Washington, D.C. 20460Mr. Roman Kuchkuda
Project Officer

DISCLAIMER

This report has been reviewed by the Office of Toxic Substances, U.S. Environmental Protection Agency, and approved for publication. Approval does not signify that the contents necessarily reflect the views and policies of the U.S. Environmental Protection Agency, nor does mention of trade names or commercial products constitute endorsement or recommendation for use.

PREFACE

This report presents the results of a study to assess and predict worker and consumer exposure to nitrilotriacetic acid in detergents.

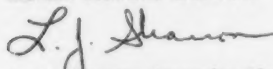
This study was performed by Midwest Research Institute, as Task IV, under Contract No. 68-01-3896 for the Office of Toxic Substances of the U.S. Environmental Protection Agency. The Office of Toxic Substances' project officer for this study was Mr. Roman Kuchkuda.

Midwest Research Institute would like to thank Ms. Justine Welch, Environmental Protection Agency, Office of Toxic Substances, for her valuable assistance during the course of this task. Her effort in providing Midwest Research Institute with industry contacts and data, as well as review comments, is sincerely appreciated. The cooperation of personnel from the Procter and Gamble Company, Monsanto Company, and W. R. Grace Company is sincerely appreciated.

Principal Midwest Research Institute contributors to this study included: Dr. Alfred F. Heiners (Task Leader), Principal Chemist; Mr. Charles Mumma, Senior Chemical Engineer; Dr. Eugene Podrebarac, Senior Chemist; Mr. Robert Peisdorf, Associate Occupational Health Scientist; Mr. Harold Owens, Associate Industrial Chemist; and Mr. Howard Gadberry, Senior Advisor for Technology. Mr. Albert E. Stewart, President, Stewart Industrial Hygiene Service, acted as consultant. Dr. Thomas W. Lapp is the project leader for this contract, under the supervision of Dr. Edward W. Lawless, Head, Technology Assessment Section.

Approved for:

MIDWEST RESEARCH INSTITUTE



L. J. Shannon, Executive Director
Environmental and Materials
Sciences Division

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SECTION 1

INTRODUCTION AND OBJECTIVES

Nitrilotriacetic acid (NTA) is being considered as a partial replacement for phosphates in detergents produced in the United States. Currently, NTA is manufactured by Monsanto and W. R. Grace, who export the material to the Canadian detergent market and supply it for use in certain industrial processes. Current Canadian household detergent products are limited to 2.2% phosphorus. The NTA content of these detergents ranges from 0 to 25%; the industry-wide average of 15% is based on total poundage of detergent and the quantity of NTA sold in Canada.

The Environmental Protection Agency (EPA) is concerned about the possible consequences of NTA use in detergents in the United States. The purpose of this investigation is (a) to assess current workplace (worker) exposure to NTA during manufacture and formulation, and (b) to predict the possible future extent of worker and consumer exposure if NTA production and use in detergents were increased to 1 billion pounds per year. Exposure by way of drinking water was not a part of this effort, nor were health or environmental effects information; these topics are under consideration in EPA.

SECTION 2

SUMMARY

A summary of the potential for exposure to NTA during manufacture, formulation, and consumer use is presented in Table 1.

HUMAN EXPOSURE DURING MANUFACTURE

The production of NTA is highly automated and is largely under remote controls. Thus, production workers have little potential for exposure to process chemicals except in the bagging and loading operations of the final product, the trisodium salt of NTA.

Production Technology

Trisodium nitrilotriacetate, the sodium salt of NTA, is currently being produced in the United States by Monsanto Chemical Company and by the W. R. Grace Company. The combined production from the Monsanto and W. R. Grace plants is currently approximately 70 million pounds of NTA per annum.

The W. R. Grace production process involves three steps: (a) the reaction of formaldehyde and ammonia to give hexamethylenetetramine (HMT), (b) the reaction of hydrogen cyanide (HCN) with HMT to give nitrilotriacetoneitrile, and (c) the hydrolysis of nitrilotriacetoneitrile by sodium hydroxide to give trisodium nitrilotriacetate. The Monsanto plant also uses this process under a licensing agreement.

Based on information provided by W. R. Grace and Monsanto, a total of only 32 workers are estimated to be involved currently in production of NTA in U.S. plants. For a projected NTA production rate of 400 million pounds per year, an estimated labor force of 57 workers would be required. A rate of 1 billion pounds per year would require 98 to 120 workers.

Analysis of Probable Worker Exposure

The entire NTA production process is automated and all regular shift workers, except those engaged in product packaging and loading activity, are normally located in a remote control room, separated from the process operations.

TABLE 1. SUMMARY OF POTENTIAL NTA EXPOSURE
FROM DETERGENT PRODUCTS

Exposure source	Potential No. of persons exposed	Potential exposure (μ g NTA/day)
NTA manufacture	98-120 ^{a/}	< 100-500 ^{b/} 8,200 ^{c/}
Detergent formulation	2,500 ^{a/}	< 338-3,380 ^{d/}
Consumer products ^{e/}		
Powdered laundry detergent		
Automatic clothes washer	176 x 10 ⁶	0.07-0.38 ^{f/}
General cleaning	176 x 10 ⁶	8.75-17.5
Residue on clothes	212 x 10 ⁶	0.44-1.28
Hand laundry and dishwashing	5 x 10 ⁶	8.75-17.5
Residue on dinnerware	6 x 10 ⁶	4.8-968
Powdered dishwashing detergent		
Automatic dishwashing	33 x 10 ⁶	0.011-0.120
Residue on dinnerware	40 x 10 ⁶	4.8-968
Light-duty detergent		
Hand dishwashing	171 x 10 ⁶	8.75-17.5
Residue on dinnerware	206 x 10 ⁶	4.8-968
General cleaning	176 x 10 ⁶	8.75-17.5

a/ Assumes NTA annual production of 1 billion pounds.

b/ Normal line workers - no respirators.

c/ Hopper car loaders - no respirators.

d/ The exposure values are "typical" and "extreme," respectively.

e/ Assumes only NTA detergents in use.

f/ Exposure values represent moderate and maximum detergent use and differences in (a) inhalation volume or (b) skin area for men, women, and children.

Air monitors located at various points in the plant area trigger an alarm in the event of any process leaks of toxic material (e.g., HCN).

Dust losses of product are apt to occur to the work atmosphere of the drying kiln, the product packaging area, and the product bulk loading operations. Therefore, the risk of worker exposure via both skin contact and inhalation appears to be greatest for these operations.

Worker Exposure Data

Actual worker exposure data have been compiled at the Monsanto facility. This study included representation of all job classifications in the plant. Urine samples were taken for analysis and the air in the breathing zone of each worker was monitored. NTA was not detected in the urine samples (detection limit, 0.5 mg/liter by gas chromatography/mass spectrometry (GC/MS)).

The highest exposure area, the hopper car loader area, had an average potential exposure of 8.2 mg NTA per 8-hr workday. In this area the workers normally wear protective clothing and equipment during periods of high exposure risk.

HUMAN EXPOSURE DURING DETERGENT FORMULATION

The Detergent Formulation Process

The use of NTA as a replacement for sodium tripolyphosphate in detergents would not require changes in the current formulating process in the United States.

The method currently being used for the commercial formulation of granular laundry detergents is primarily a batch process, in which raw ingredients are pumped or conveyed through a closed system to reactors and mixers, and then blended into a slurry. The slurry is sprayed from the mixer into drying towers to achieve the desired granulation size and moisture content. The finished powder is then conveyed to production lines where it is automatically put into cartons and packed for shipping.

Liquid laundry detergents and powdered cleansers are also formulated primarily by batch processes in a closed system.

Areas of Exposure in Detergent Plants

The workplace atmosphere can become contaminated with detergent dust containing NTA from abnormal events such as leaks in the product lines and spills caused by a malfunction in equipment; routine and nonroutine equipment cleanup operations can also contribute to worker exposure. Operations which require manual handling of bags of NTA and the filling and packing production lines

can become high dust areas, particularly when powder is spilled as a result of machine jams and product changeovers. In these situations, worker exposure can be controlled by protective clothing.

Worker Exposure

The number of production workers that would be directly exposed to NTA from the manufacturing of laundry and dishwashing detergents in the United States is estimated to be 2,500. The use of NTA would not change the number of workers required to produce detergents at the present market level.

Typical occupational exposure to NTA via airborne detergent dust during detergent formulation has been estimated to be $< 4.8 \mu\text{g}/\text{NTA}$ per kilogram per day for an adult male and $< 3.6 \mu\text{g}/\text{NTA}$ per kilogram per day for an adult female. This assumes that (a) all the dust is detergent; (b) NTA comprises 25% of the detergent; and (c) 10% of the dust is respirable.

CONSUMER EXPOSURE TO DETERGENTS

Consumer exposure to detergents can result from inhalation of detergent dust, percutaneous absorption from contact with wash water or direct skin contact with the detergent, ingestion of residue on dishes or utensils, and skin contact with residues in clothing.

Number of Consumers Exposed

Laundrying Operations--

The number of people in the United States that would be exposed to NTA while doing laundry has been estimated to be 174 million or 81% of the total population if only NTA-containing detergents were available.

Dishwashing Operations--

An estimated 2 million households in the United States use laundry detergents for dishwashing by hand. If each person in the household over 10 years of age washes dishes at sometime, a maximum of 5 million persons would be exposed.

If NTA were used in automatic dishwashing detergents, an estimated 33 million persons would be exposed.

If NTA were used in light duty detergents, an estimated 174 million persons would be exposed since even those households with automatic dishwashers wash dishes (and other kitchen utensils) by hand at sometime.

Residues in Clothing--

Virtually everyone in the United States whose clothes were washed with NTA-containing detergents would be exposed via this route.

Residues on Dinnerware--

An estimated 5.8 million persons would be exposed following hand washing of dishes with an NTA laundry detergent, 40 million persons exposed following dishwashing in an automatic dishwasher, and 214 million persons exposed following hand washing of dishes with a light duty detergent.

Extent of Exposure

Typical consumer exposure to NTA from inhalation of detergent dust has been estimated to be 0.001 μg NTA per kilogram per day (54 kg adult). Exposure to NTA via percutaneous absorption from washing dishes (or laundry, etc.) by hand has been estimated to be 0.13 $\mu\text{g}/\text{kg}/\text{day}$ (70 kg adult) for a 1/2-hr exposure. The estimated exposure from NTA residues in clothes is 0.018 $\mu\text{g}/\text{kg}/\text{day}$ (70 kg adult). Exposure by ingestion of NTA from dinnerware has been estimated to be 0.07 $\mu\text{g}/\text{kg}/\text{day}$ (70 kg adult) for rinsed and towel-dried dishes.

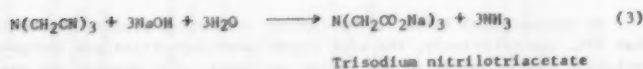
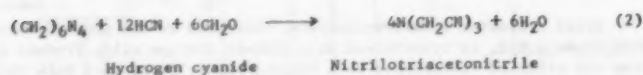
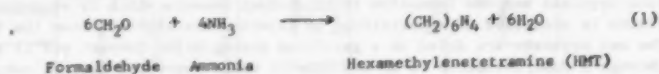
SECTION 3

HUMAN EXPOSURE DURING MANUFACTURE

PRODUCTION TECHNOLOGY FOR TRISODIUM NITRILOTRIACETATE

Trisodium nitrilotriacetate, the sodium salt of NTA, is currently being produced in the United States by Monsanto Company at the Chocolate Bayou Plant near Alvin, Texas, and by the W. R. Grace Company at Nashua, New Hampshire. The combined annual production of the Monsanto and Grace plants is currently at a level of approximately 70 million pounds. Monsanto apparently ships all of its product to Canada for use in detergents. Most of the W. R. Grace Company product is also shipped to Canada, and most of the remainder* is used industrially in the United States. According to information provided by a spokesman for W. R. Grace (Huber, 1978b), Canada currently consumes about 60 million pounds per year of trisodium nitrilotriacetate (i.e., the sum of shipments to Canada from Monsanto and W. R. Grace in the USA). Based on this information, the current use of NTA in the United States can be estimated at 10 million pounds of NTA per year.

The basic process chemistry for the W. R. Grace process according to Huber (1978b) is described by the following chemical reactions.



* Two divisions of W. R. Grace (in Sweden and in England) purchase "relatively modest" amounts (compared to the total NTA production of W. R. Grace) of trisodium nitrilotriacetate for use in detergents and specialty applications (Amirsakis, 1979).

A representative flow diagram of the W. R. Grace production process for trisodium nitrilotriacetate is presented in Figure 1. The Monsanto plant for trisodium nitrilotriacetate manufacture also uses this W. R. Grace process (with some minor modifications involving principally the type of material conveying equipment) under a licensing agreement (Huber and Amirsakis, 1978).

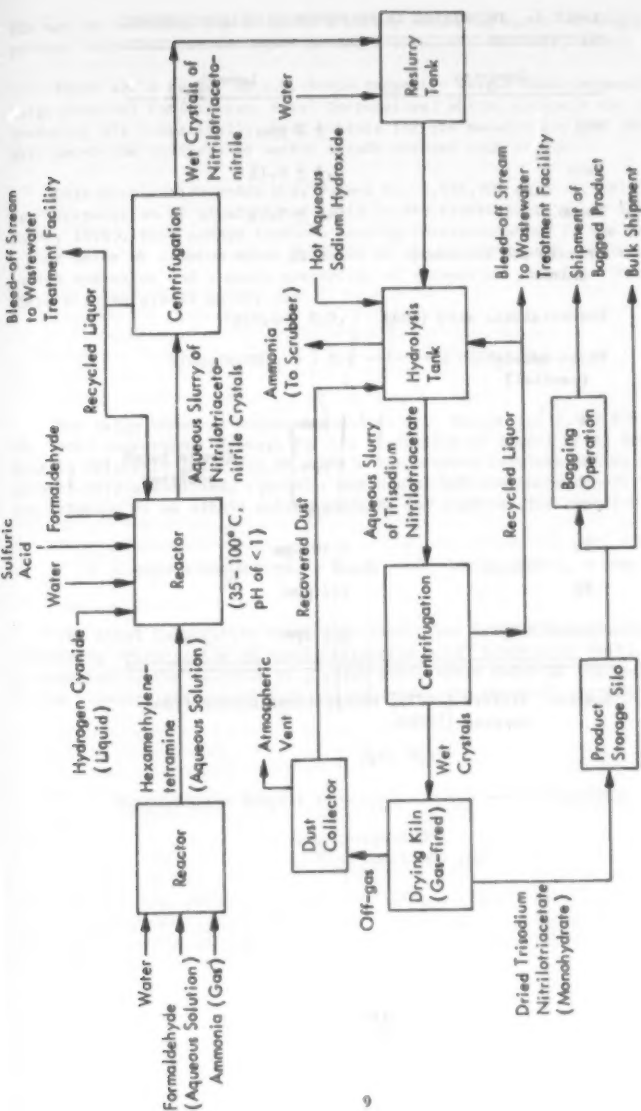
In the first reaction step, formaldehyde in aqueous solution reacts with gaseous ammonia to form a condensation product known as HMT. The yield for this reaction is essentially quantitative. This operation is commonly conducted as a batch operation in a closed system to maintain a supply of HMT.

In a typical operation, an aqueous solution of HMT is added to an aqueous solution containing HCN, formaldehyde, and sufficient acid (sulfuric acid) to maintain the pH of the reaction mixture below 1. The reaction is conducted in the temperature range of 35 to 100 C. The reaction product, consisting of a slurry of nitrilotriacetonitrile crystals, is processed in a centrifuge to separate the crystals from the liquor. The separated liquor is recycled to the reactor.

Wet crystals of nitrilotriacetonitrile discharged by the centrifuge are agitated with water in a reslurry tank to form a slurry. This slurry is added to a hot aqueous solution of caustic soda to hydrolyze the nitrile functions. This reaction results in the formation of a slurry of trisodium nitrilotriacetate crystals and the formation of by-product ammonia which is recovered. This slurry is processed in a centrifuge to separate the crystals from the liquor. The wet crystals are dried in a gas-fired drying kiln. Exhaust gas is passed through a dust collector to an atmospheric vent; recovered dust is recycled to the hydrolysis tank.

Dried trisodium nitrilotriacetate, recovered as the monohydrate, $N(CH_2CO_2Na)_3 \cdot H_2O$, is transferred to a product storage silo. Product is removed from the silo and transferred to a bagging operation or to a bulk shipment station where the material is loaded into hopper bottom railroad cars.

As indicated in Table 2, the typical commercial product purity is greater than 99%. Quantitatively, the most significant impurities are inorganic salts, including sodium hydroxide and sodium carbonate. Also present are small quantities of iminodiacetic acid (IDA). The other impurities such as HCN and trace metals are present at low parts-per-million levels (Winters, 1977). In response to a Midwest Research Institute (MRI) question, a formaldehyde analysis was performed by Monsanto on a plant sample which indicated that the product contained at most 2 ppm formaldehyde (i.e., in the analytical test, any material that releases formaldehyde in acid will give a positive response). Once NTA is formulated into a detergent, it has little tendency to degrade. Under carton/shelf exposure conditions of moisture and air, NTA is completely stable. P&G Canada routinely monitors its NTA-containing detergents (a) as made, (b) in the warehouse, and (c) in the trade; no measurable degradation has been detected.



Source: Huber, 1978 B.

Figure 1. General schematic for commercial production of trisodium nitrioltriacetate.

TABLE 2. IMPURITIES IN TRISODIUM NITRILOTRIACETATE

Impurity	Level	
HCN	4 ± 2 ppm	
NaOH	$0.3 \pm 0.1\%$	
Na_2CO_3	$0.4 \pm 0.1\%$	
Primary and secondary amines	$\sim 0.2\%$	
Iminodiacetic acid (IDA)	$(0.2 \pm 0.05\%)$	
Trace metals (partial)		
K	6 ppm	} single batch analyses
Zn	2 ppm	
Cu	1 ppm	
Fe	< 10 ppm	
Pb	1-2 ppm	
Formaldehyde	≤ 2 ppm	

Sources: Winters (1977), except formaldehyde from Hopping (1978).

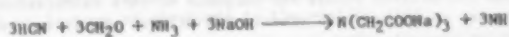
NTA may be oxidised, but it takes a strong oxidizing agent--stronger than present components in detergent products using NTA (Winters, 1978).

There are a number of U.S.-based companies (e.g., Olin Corporation, Geigy Chemical Corporation, Ethyl Corporation) which, although not presently producing NTA domestically, hold patents for its manufacture and could presumably enter the business if market trends warrant such action.

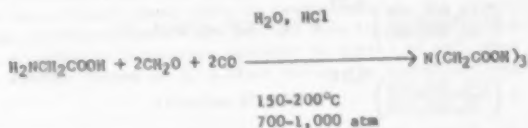
Olin Corporation holds U.S. Patent No. 3,578,709 (May 11, 1971) concerning "Preparation of Alkali Metal Salts of Nitrilotriacetic Acid" (Bishop and Jache, 1971). This method involves heating triethanolamine in the presence of a zinc oxide or cadmium oxide catalyst at 150 to 300°C with a mixture of sodium hydroxide and a minor proportion of potassium hydroxide. The reaction, where M is an alkali metal, is:



The Geigy Chemical Corporation holds U.S. Patent No. 3,415,878 (December 10, 1968) concerning "Process for the Production of Alkali Metal Salts of Nitrilo Triacetic Acid" (Gaunt, 1968). The process involves adding an aqueous, mineral-acid-stabilized, equimolar mixture of HCN and formaldehyde to an aqueous solution of an alkali metal hydroxide and ammonia. The reaction is:



The Ethyl Corporation holds U.S. Patent No. 3,470,245 (September 30, 1969) concerning "Preparation of Nitrilotriacetic Acid" (Jackisch, 1969). The NTA is prepared by the reaction of glycine with carbon monoxide and formaldehyde in the presence of aqueous hydrogen chloride. The chemical reaction is:



ESTIMATED NUMBER OF U.S. PRODUCTION WORKERS FOR NTA

Based on information provided by the manufacturers, the total U.S. plant labor force currently involved in production of NTA is estimated to be 32 workers.

The total number of plant workers required for levels of production larger than 50 million pounds annually can be estimated as follows. Peters and Timmerhaus (1968) have indicated that a "one-fourth factor" can be used to scale up labor requirements from one plant size to a larger plant size. This factor takes into account the fact that larger plant sizes require less than proportional labor forces because of economies of scale.

For a projected NTA production rate of 400 million pounds NTA per year, there would probably be two plants each with production rates of 200 million pounds per year. On this basis, the estimated number of workers required is:

$$2 \times \left(\frac{200,000,000}{50,000,000} \right)^{0.25} \times 20 \text{ workers} = 2.83 \times 20 = 57 \text{ workers}$$

An industry source stated that a production facility with an annual capacity of 300 million pounds would be considered an ideal size based on an optimum size hydrogen cyanide generation plant of 100 million pounds annual capacity. Therefore, MRI chose to limit the annual production capacity of any one plant to no more than 350 million pounds for purposes of this calculation. Thus, the estimated manpower requirement to produce 400 million pounds per year is 57 workers per 24-hr operating day.

If annual production were increased to 1 billion pounds per year, there would probably be three or four plants whose individual total production capacity would average 250 to 350 million pounds per year. Based on the above assumptions, the required labor force per 24-hr operating day is equal to:

$$4 \left(\frac{250,000,000}{50,000,000} \right)^{0.25} \times 20 = 120 \text{ workers, or}$$

$$3 \left(\frac{350,000,000}{50,000,000} \right)^{0.25} \times 20 = 98 \text{ workers.}$$

Thus, the projected labor force for the three production levels is as follows: 70 million pounds (current level) requires 32 workers; 400 million pounds would require 57 workers; and 1 billion pounds would require 98 to 120 workers.

ANALYSIS OF PROBABLE WORKER EXPOSURE TO NTA IN MANUFACTURING OPERATIONS

An analysis of the processing unit operations used in manufacturing NTA was presented in Figure 1.

The entire production process is automated and all workers, except those engaged in product packaging and loading activity, are provided with a remote control room where they spend much of their time in data monitoring and recording activity separated from the process operations. The automatic plant features include process sampling, process material weighing, and transfer and conveying equipment. Air monitors located at various points in the plant area trigger an alarm in the event of any process leaks of toxic material (e.g., HCN).

The first process step involves the reaction of formaldehyde with ammonia to form HMT. The risk of worker exposure in this step appears to be minimal since the reaction is carried out by remote control and the equipment is monitored for gas leaks. The HMT is discharged as an aqueous solution, thus minimizing the possibility of work area contamination with airborne dusts containing process chemicals.

The second reaction step and the subsequent centrifuging step are conducted in a closed system, primarily because of the involvement of highly toxic HCN. Therefore, the risk of worker exposure to reactants, NTA contaminants, or by-products in the operating area for these operations appears to be negligible with the exception of special but controllable exposure hazards which could be created by equipment failure (i.e., breakdown or rupture of equipment resulting in spills or leakage of chemicals to the working area).

The transfer of crystals of nitrilotriacetonitrile from the centrifugation step to the reslurry step is also carried out by remote control, thus restricting worker contact. It appears that the degree of potential exposure in this area would probably be quite low because the crystals are wet and therefore unlikely to create any dust problems.

In the hydrolysis and centrifugation steps, all process operations are carried out in a liquid phase again by remote control. The separated crystals of trisodium nitrilotriacetate are wet and thus the prospects for generation of dust (i.e., skin or inhalation exposure to dusts) in this area appear to be remote. Ammonia formed as by-product during the hydrolysis reaction is recovered.

The wet crystals are dried to produce a powdered product. In the drying step, the off-gas containing fuel combustion products, water vapor, and some dust (sodium salt of NTA) is passed through a dust collector and then vented to the atmosphere. Dust recovered by the dust collector is transferred to the hydrolysis tank for reprocessing.

Dust losses of product are apt to occur to the work atmosphere of the drying kiln, the product packaging area, and the product bulk loading operations. Therefore, the risk of worker exposure via both skin contact and inhalation appears to be greatest for these operations.

In summary, the potential for exposure to NTA during the various steps in the manufacturing process is as follows:

<u>Manufacturing step</u>	<u>Potential for NTA exposure</u>
Formation of HMT	Negligible
Reaction of HMT with HCN	Negligible
Centrifugation and reslurry	Negligible
Hydrolysis and centrifugation	Negligible
Drying	Very large if no precautions employed
Packaging and bulk shipment	Very large if no precautions employed

Proper precautions which can significantly reduce the exposure risk in high exposure operations include:

- Adequate ventilation and dust control equipment.
- Use of proper protective apparel by workers, e.g., gloves, impervious work clothing, and filter masks, or airline breathing masks.

The Monsanto and Grace companies both report that their plants observe these safety precautions.

In summary, since the production of NTA is highly automated and operated by remote control, production workers have a high exposure potential to only the trisodium salt of NTA--the final product--in the bagging and loading operations if protective apparel is not worn. The final product is of at least 99% purity; the contaminants are HCN (4 ppm), sodium hydroxide (0.3%), sodium carbonate (0.4%), primary and secondary amines (0.2%), formaldehyde (≤ 2 ppm), and trace metals (see Table 2, p. 10).

WORKER EXPOSURE DATA

Actual worker exposure data have been compiled at the Monsanto (Chocolate Bayou) facility (Hill et al., 1977). Urine samples were taken for analysis, and air in the breathing zone of each worker was monitored.

Two 24-hr urine samples were collected from each NTA plant worker. Each sample was collected over the 24-hr period approximately in the middle of the workweek. The two samples were taken at approximately 1-week intervals. NTA

was not detected in the urine samples (by GC/MS) at or above the limit of detection 0.5 mg/liter.

Monsanto (Hill et al., 1977) assumed that, since the "metabolism of NTA occurs with excretion of a significant portion (mean value 13%)^a of unchanged NTA in urine," urinary levels could be used to measure the exposure to NTA. A 12.3% mean value was reported by Budny and Arnold (1973) who administered 10 mg of NTA orally, in a single dose, to human volunteers; the dose level varied from 0.107 to 0.161 mg/kg. A mean of $12.33 \pm 7.41\%$ of the administered NTA was excreted unchanged in the urine by the subjects. Based upon the 13% excretion level, and assuming that NTA concentrations in the urine were at the minimum detectable level, Monsanto calculated maximum daily intakes which ranged from < 1.69 to < 13.86 mg.

An important question is the validity of using the 13% value for the excretion level; in the Budny and Arnold study, human volunteers received 10 mg orally at one time; however, the air analyses (described later) indicate that the workers were ordinarily exposed by inhalation to 0.1 to 0.5 mg during the entire course of an 8-hr work shift. The lower intake level and the different route of administration could result in substantially different absorption and excretion rates and quantities.^b If so, there could be wide variation in the level of exposure which could be detected by urinalysis. For example, if none of the NTA were absorbed or excreted following inhalation, then urinalysis would be incapable of measuring the extent of exposure; if only 1% of the NTA were excreted following inhalation, then exposures of up to 180 mg could not be distinguished from zero exposure.^c

^a The mean figure stated in the paper by Budny and Arnold was 12.33% in the urine and 76.99% in the feces.

^b Consultations concerning this question were held with Dr. C. C. Lee, Deputy Director of the Pharmacology and Toxicology Department, Dr. Harry V. Ellis III, Senior Pharmacologist, and Dr. Betty L. Herndon, Associate Pharmacologist, all of NRI. The consensus of opinion was that, in the absence of additional data, one should not assume that 10 mg oral doses and 0.1 mg inhalation doses would result in comparable quantities or rates of NTA excretion. The absorption mechanisms are markedly different and the distribution and excretion patterns could be significantly different.

^c The upper limit of < 13.86 mg for the daily intake of NTA was calculated by Monsanto (Hill et al., 1977) as follows: urine volume (l) x urine concentration (mg/l) $\div$ 0.13. Substituting 0.01 (1%) for 0.13 yields a daily intake of < 180 mg.

In the air analyses, full period breathing zone monitoring of each worker was performed during the 8-hr shift for which the 24-hr urine sample was collected. "Potential inhalation exposures"^{a/} ranged from 0.1 to 8.2 mg NTA per shift with a minimum quantitative level of 0.1 mg NTA per day. There were three distinct levels of NTA in the air samples. In the "normal" line area,^{b/} exposure levels of 0.1 to 0.5 mg NTA per day were usually found. The highest potential exposure was to the hopper-car loader with normal exposure periods of only 30 to 60 min/day. The hopper-car loader had a potential exposure of 8.2 mg NTA per shift. (This potential exposure assumes that the hopper-car loader does not wear a respirator; however, a respirator is required for this operation.) There was one intermediate level of exposure (maximum exposure potential of 5.7 mg/day) which occurred during a plant electrical outage (caused by a rain storm), during which NTA had to be manually removed from carrier belts, and the resulting spills in this area were hosed down the drain.

As shown, calculations based upon the Monsanto data indicate that the worker with the highest potential in inhalation exposure is the hopper-car loader.

Area	Potential exposure ^{a/} (mg NTA/shift)	Time-weighted average concentration ^{b/} (mg NTA/m ³)	Average concentration during shift ^{c/} (mg NTA/m ³)
Normal line area	< 0.1-0.5 ^{d/}	< 0.01-0.05	< 0.01-0.05
Hopper-car loader	8.2	0.82	6.56
During plant outage	5.7 max.	0.57 max.	0.57 max.

^{a/} From Hill et al. (1977).

^{b/} MRI calculations. Time-weighted average concentration (mg NTA/m³) equals potential exposure ÷ 10 m³ (standard workday tidal volume).

^{c/} MRI calculations. The actual exposure time for the hopper-car loader was reported to be 30 to 60 min (Hill et al., 1977) and for the purpose of this estimation was presumed to be 1 hr. The other exposure periods were 8 hr (Ward, 1979).

^{d/} The mean potential exposure was < 0.2 (Plunkert, 1979).

^{a/} "Potential inhalation exposures" were calculated by Monsanto (Hill et al., 1977) based on the time-weighted average concentration of NTA in the air the standard workday tidal volume. It was assumed that the worker had no respiratory protection and that no inhaled NTA was exhaled.

^{b/} Of the three areas in which NTA exposures were measured, the "normal" line area represents all areas other than the area where the hopper-car loader works (Ward, 1979).

The relatively very high concentrations of NTA in the area of the hopper-car loader can also be estimated from other data as follows: Hill et al. (1977) reported that the respirator of the hopper-car loader contained 4.5 mg NTA on one occasion and 7.8 mg NTA on another. If the NTA in the respirator represents the amount collected during a single exposure period (1 hr), the average concentration of NTA in the air can be calculated by assuming that the amount of NTA in the respirator was equal to the amount of NTA in the air inhaled by the worker during the 1-hr exposure period (one-eighth of the standard workday tidal volume, 1.25 m^3). Thus the calculated average NTA concentrations are:

$$\frac{4.5 \text{ mg}}{1.25 \text{ m}^3} = 3.6 \text{ mg/m}^3 \quad \text{and} \quad \frac{7.8 \text{ mg}}{1.25 \text{ m}^3} = 6.2 \text{ mg/m}^3$$

These figures are in general agreement with the calculated level 6.56 mg/m^3 .

The following data concerning the exposure of NTA production workers to other products were provided by Monsanto (Metcalf, 1978b).

Ammonia - The American Conference of Governmental Industrial Hygienists (ACGIH) limit is 25 ppm (time-weighted average).

A series of area measurements in the highest exposure potential zones using long-term detector tubes showed ambient concentrations generally below 10 ppm. Considering the limited exposure time of operators in such areas, worker exposures on an 8-hr basis have been calculated to be less than 1.0 ppm time-weighted average. A 10-fold variation in airborne concentrations versus worker time-weighted average exposure is not uncommon in processes having dynamic work patterns.

HCN - The ACGIH limit is 10 ppm (ceiling).

Utilizing long-term detector tubes specific for HCN, the environmental concentrations are for the most part less than the lower detection limit of 0.25 ppm. HCN is handled in completely contained systems where even minor leakage cannot be tolerated. Routine exposure to operators is nil.

Two continuous HCN monitors are located in the NTA unit to alert personnel of possible emergency situations. Both units are set to alarm at 6 ppm.

Formaldehyde - The ACGIH limit is 2 ppm (ceiling).

The exposure information on formaldehyde is more subjective. Formaldehyde, while quite irritating at high concentrations, can be easily recognized at airborne concentrations of 1.0 ppm and detected by experienced personnel at

somewhat lower levels.^{b/} Monitoring surveys in formaldehyde handling areas using impinger collection followed by colorimetric analysis have substantiated these odor/effect properties.

While little objective monitoring data on formaldehyde exposure in the Monsanto process have been developed to date, the observations and judgment of the plant professionals indicate trace odors of formaldehyde being present in highest potential exposure areas.^{b/} Area monitoring is scheduled to confirm our assessment of worker exposures being less than the 2.0 ppm ceiling and certainly less than 0.5 ppm on a TWA basis.

^{a/} Mr. J. S. Metcalf, Manager, Product Acceptability, Detergents and Phosphates Division, was contacted by Dr. Alfred F. Meiners on June 26, 1979; he stated that the experienced personnel to whom he was referring were not sensitized to formaldehyde, but had simply become skilled in recognizing formaldehyde at concentrations below 1 ppm.

^{b/} Mr. J. S. Metcalf, Manager, Product Acceptability, Detergents and Phosphates Division, was asked about these areas on February 9, 1979, by Dr. Alfred F. Meiners. Mr. Metcalf said that sampling for formaldehyde was done at a variety of locations throughout the plant. Although he did not remember the exact layout of the plant, he knew that the sampling was done in a number of areas where one would reasonably expect to detect formaldehyde, such as in areas where the reactor was opened and closed.

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SECTION 4

HUMAN EXPOSURE DURING DETERGENT FORMULATION

DESCRIPTION OF DETERGENT FORMULATION PROCESS

The method currently being used for the commercial formulation of granular detergents is primarily a batch process. In the making of powdered detergents, raw ingredients, stored in tanks or bins, are pumped or conveyed through a closed system to reactors and mixers and then blended into a slurry. The slurry is sprayed from the mixer into drying towers to achieve the desired granulation size and moisture content. Additional raw materials can also be added after the drying process. The finished powder is then conveyed to production lines where it is automatically put into cartons and packed for shipping. The industry-wide level of NTA used in powdered detergent currently averages 15% in Canada, where a nationwide limit of 2.2% phosphorus is in effect.

Powdered cleansers are also formulated primarily by a batch process. These products are dry mixes which contain small quantities of detergents. The filling and packing production lines for cleansers can be major sources of dust contamination, particularly in the can filling operation. Liquid laundry detergents are also formulated primarily by a batch process in a closed system. The major steps in this operation include pumping the raw materials from storage tanks into mixers. After mixing, the liquid is bottled and packed by automatic equipment.

AREAS IN EXPOSURE IN DETERGENT PLANTS

The workplace atmosphere can become contaminated with detergent dust containing NTA from abnormal events such as leaks in the product lines and spills caused by a malfunction in equipment; routine and nonroutine equipment cleanup operations can also contribute to worker exposure. Operations which require manual handling of bags of NTA, and the filling and packing production lines can become high dust areas, particularly when powder is spilled as a result of machine jams and product changeovers. In these situations, worker exposure can be controlled by protective clothing.

NUMBER OF WORKERS EXPOSED

The total number of production workers in the entire soap and detergent industry in 1976 was 23,400 (Department of Labor, 1976). The total number of production workers that would be directly exposed to NTA from the manufacture of laundry and dishwashing detergents in the United States is estimated to be less than 2,500. The use of NTA would not change the number of workers required to produce detergents at the present market level.

Procter and Gamble has "somewhat over 1,000 workers" involved in the manufacture of detergents in the United States, and their estimate of current industry-wide exposure to NTA is double that figure, or approximately 2,000 (Winters, 1978a). About 70% (or roughly 700) of the Procter and Gamble workers are involved in the manufacture of granular laundry detergents. Furthermore, only about one-half of these workers enter the dustiest areas of detergent manufacture which are the areas where the detergents are moved, boxed, or packaged (Hopping, 1979).

EXPOSURE LEVELS

Occupational exposure to airborne dust (measured as total dust) during detergent formulation has been measured (Winters, 1978b). The total dust level, as a time-weighted average, was $1.38 \mu\text{g}/\text{liter}$ ($1.38 \text{ mg}/\text{m}^3$). This figure is an average proportioned by the time spent in the three dustiest areas associated with detergent manufacture. The range of concentrations for these three areas (in micrograms per liter) are: 2.33, 1.11, and 0.67 (Hopping, 1978). It was assumed that a worker spends one-third of his time^{a/} in each area. On the basis of these dust levels, the estimated NTA inhalation exposure was calculated (Winters, 1978b) to be:

Person exposed	Exposure ($\mu\text{g Na}_3\text{NTA}/\text{kg}/\text{day}$)	
	Typical	Extreme
Adult male (70 kg)	< 4.8	48.3
Adult female (54 kg)	< 3.6	35.7

^{a/} These three areas of higher dust concentrations are those in which the detergent is moved, boxed, or packaged. The average of these three concentration levels ($1.38 \mu\text{g}/\text{liter}$) provides a time-weighted average concentration assuming that a worker spends an equal time in each area. Procter and Gamble believes that this assumption is reasonable; the areas are in close proximity and workers do actually spend approximately one-third of their time in each area (Hopping, 1979).

The calculations were made as follows:

*Breathing rate

$$\text{Adult male (70 kg), light work } \frac{17.1 \text{ breaths}}{\text{min}} \times 1.673 \frac{\text{l}}{\text{breath}} = 28.6 \text{ l/min}$$

(tidal volume) (Biology Data Book, 1974).

$$\text{Adult female (54 kg), light work } \frac{19 \text{ breaths}}{\text{min}} \times 0.860 \frac{\text{l}}{\text{breath}} = 16.3 \text{ l/min}$$

(tidal volume) (Biology Data Book, 1974).

$$\text{*Exposure time} = 8 \text{ hr/day} \times 5 \text{ days/week} = 40 \text{ hr/week.}$$

$$\text{Per day, weekly basis} = 40 \text{ hr/week} \times 1/7 \text{ day/week} = 5.71 \text{ hr/day.}$$

The 5.71 hr/day exposure time is on a weekly basis to be comparable to the other estimated exposure.

*Estimated exposure

$$\text{Adult male } \frac{1.38 \text{ } \mu\text{g/l} \times 0.25^a \times 28.6 \text{ l/min} \times 60 \text{ min/hr} \times 5.71 \text{ hr/day}}{70 \text{ kg}} =$$

$$48.3 \text{ } \mu\text{g/kg/day.}$$

$$\text{Adult female } \frac{1.38 \text{ } \mu\text{g/l} \times 0.25^a \times 16.3 \text{ l/min} \times 60 \text{ min/hr} \times 5.71 \text{ hr/day}}{54 \text{ kg}} =$$

$$35.7 \text{ } \mu\text{g/kg/day.}$$

These exposure estimates assume that all the measured dust is detergent, that 100% of the dust is respirable, that all of the inhaled dust remains in the body, and that the 7-day breathing rate is that corresponding to light work. These estimates were shown previously as the extreme exposure levels. Industry sources believe that at most no more than 40% of the dust is respirable, and that in reality < 10% would be respirable. Estimates based on the < 10% figure are shown above as the typical exposure levels.

In our opinion, the Procter and Gamble calculations provide a reasonable estimate of average occupational exposure to NTA in the dustiest areas of detergent manufacture. The calculations were made for a plant actually using NTA for which an average dust level of 1.38 $\mu\text{g/liter}$ was determined. Recent data (Hopping, 1979) indicate that time-weighted average dust levels in these areas in U.S. plants are less than 1 $\mu\text{g/liter}$. Also, a 25% content of NTA in the

^{a/} A 25% content of NTA in the detergent is assumed. This would represent maximum concentrations.

detergent is used in the calculations; actual NTA content in Canadian detergent ranges from 0 to 25% with an average of 15% (Brownridge, 1978). Furthermore, in all of the studies, total dust levels were measured, and some of this dust is known to be material other than detergent (Hopping, 1979).

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SECTION 5

CONSUMER EXPOSURE TO DETERGENTS

The total consumer exposure^{a/} to detergents includes exposure from:

- Inhalation of detergent dust in home uses.
- Percutaneous absorption from contact with wash water including laundry, dishwashing, and other operations such as mopping floors and general cleaning.
- Percutaneous absorption from skin contact with detergent when measuring detergent, handling the box of detergent, or cleaning a spill of detergent.
- Percutaneous absorption from skin contact with residues in clothes.
- Ingestion of residues left on dishes and utensils.

NUMBER OF CONSUMERS EXPOSED

A summary of the number of consumers potentially exposed to NTA while using selected detergents is presented in Table 3. The underlying assumption of these figures is that all consumers would use NTA-containing products and none would use non-NTA products.

Laundering Operations

The primary exposure from the use of NTA laundry detergents would occur while performing laundering operations. (Subsequent exposures may occur from residues on clothes.) The number of people in the United States that could be exposed to NTA while doing laundry has been estimated to be 176 million (MRI estimate). This figure is based on the estimate that all members of a household over 10 years of age are likely to operate a washing machine at some time (AIAA,

^{a/} Another broad segment of the general public would be exposed to NTA in the marketing, transportation, and warehousing of detergents. No attempt was made to estimate the number of persons involved in these operations and no data were available to estimate the extent of their exposure.

TABLE 3. POTENTIAL NUMBER OF CONSUMERS EXPOSED TO NTA VIA DETERGENT USAGE

Product	Use	Route(s) of exposure	Potential No. persons exposed Total ^a	Most often exposed	Remarks
Powdered laundry detergent	Automatic clothes washer	Inhalation	176×10^6	76×10^6 ^b	Based on total number of households
	General cleaning and hand laundry	Percutaneous and inhalation	176×10^6	76×10^6 ^b	
	Residue on clothes	Percutaneous	212×10^6	212×10^6	Based on total U.S. residential population
	Hand dishwashing	Percutaneous and inhalation	5×10^6	2×10^6 ^b	
	Residue on dinnerware ^c	Ingestion	6×10^6	6×10^6	Based on estimated 14×10^6 households with automatic dishwashers
Powdered dishwashing detergent	Automatic dishwashing	Inhalation	33×10^6	14×10^6 ^b	
Light duty detergent (liquid)	Residue on dinnerware	Ingestion	40×10^6	40×10^6	Based on number of households using liquid detergent for same type of dinnerware cleaning Total U.S. residential population minus those using powdered laundry detergent
	Hand dishwashing	Percutaneous	171×10^6	80×10^6 ^b	
	Residue on dinnerware	Ingestion	208×10^6	206×10^6	
	General cleaning and hand laundry	Percutaneous	176×10^6	76×10^6 ^b	

^a/ Assumes that only NTA detergents are in use and that everyone in household over 10 years of age uses the detergent product at some time.

^b/ Industry estimates assuming one person per household uses the detergent product.

^c/ Dinnerware includes kitchen utensils.

1978). The Statistical Abstracts compiled by the U.S. Department of Commerce (1978) show the number of households (74.1 million), the average size of the household (2.86 persons), and the percentage of the population over 10 years of age (calculated to be 83%).

However, an industry source estimates that there are only 76 million persons who actually do laundry. This figure is based on the number of households (76 million) and assumes that one person per household does the laundry.^{a/} The MRI estimate represents the total number of persons exposed, while the industry estimate represents the number of persons who are most often exposed. (One person per household probably does laundry more often than other household members.)

Dishwashing Operations

In addition to laundry exposure, consumers may be similarly exposed when laundry detergents are used for dishwashing. An industry source estimates that 2 million households in the United States use laundry detergents for dishwashing by hand. Assuming that everyone in the household over 10 years of age washes dishes at sometime, a maximum of 5 million persons would be exposed via this route.

Currently, NTA is not used in any dishwashing detergents in the United States or Canada (Winters, 1978b); however, the potential for the use does exist.

Automatic Dishwashers--

If NTA were used in automatic dishwashing detergents, the primary exposure would occur while pouring and handling the detergent prior to actual operations. (Subsequent exposure may occur from residues on dishes.) An estimated 33 million persons would be exposed to NTA while using an automatic dishwasher. This figure is based on an estimated 14 million households in the United States with automatic dishwashers, an average of 2.86 persons per household, and an assumption that everyone in the household over 10 years of age will use the dishwasher at some time (MRI estimate). However, an industry source estimates that only one person per household uses the dishwasher; consequently, an estimated 14 million persons would be exposed. The MRI estimate represents the total number of persons exposed, while the industry estimate represents the number of persons who are most often exposed. (One person per household probably uses an automatic dishwasher more often than other household members.)

^{a/} Note that the estimates made by industry and by MRI pertaining to the number of households in the United States and the average size of a household are not identical; however, the difference is not significant.

Hand Dishwashing--

If NTA was used in a light duty liquid detergent for dishes, an estimated 171 million persons would be exposed via percutaneous absorption. This estimate is based on the following data:

- * 74.1×10^6 total households
- * 2.86 persons per household; 83% over 10 years of age
- * 14×10^6 households with automatic dishwashers
- * 2×10^6 households use laundry detergent for hand dishwashing

MRI assumed that all households, except those using laundry detergent, will wash dinnerware (including kitchen utensils) by hand and that everyone in the household over 10 years of age will be involved. The estimate includes households with automatic dishwashers, since even persons with these machines are likely to wash dishes or kitchen utensils by hand at some time.

An industry source estimates that only 60 million persons would be exposed on a regular basis to NTA from a light duty detergent. This estimate is based on the assumption that only one person per household does dishes, 76 million households, and the same data given earlier for laundry detergent use and automatic dishwashers (2 million and 14 million). It was further assumed that households with automatic dishwashers would not wash any dishes or kitchen utensils by hand.

Currently, most light duty detergents are liquid, so that the potential for exposure via inhalation would be minimal. However, the potential for dermal exposure would remain.

Residues in Clothing

Exposure to NTA also occurs from residues in clothes following laundering. Although this exposure is less than when doing laundry, virtually everyone in the United States would be exposed via this route.

Residues on Dinnerware

Exposure to NTA would also occur from residues on dinnerware following dishwashing with an NTA laundry detergent, automatic dishwashing detergent, or light duty detergent if NTA were used in these products. An estimated 6 million persons would be exposed (2.86 persons per household $\times$ 2 million) following hand dishwashing with laundry detergent; 40 million persons (2.86 persons per household $\times$ 14 million) exposed following dishwashing in an automatic dishwasher; and 206 million persons exposed following hand washing of dishes with a light duty detergent. (Note: Even those households with automatic dishwashers wash dishes and utensils by hand at some time.)

Hand Washing, Mopping, and General Cleaning

Currently, powdered laundry detergents are used for some general cleaning, as well as for washing of clothes. In addition, the use of NTA in cleansers and light duty detergents used for hand washing, mopping, and general cleaning may be considered in the future (industry source, 1978).

Use of detergents containing NTA, intended for general cleaning, would result in the exposure of 176 million persons (MRI estimate). This figure was calculated as before, based on the assumption that everyone in a household over 10 years of age might do hand washing of clothes or general cleaning at some time.

EXTENT OF EXPOSURE

Consumer exposure to NTA if used in detergent products in the United States is most likely to occur during actual use of the product; significantly less exposure is expected from contact with any residues remaining on those items washed in the detergent. A summary of human exposure to NTA through consumer use of detergent products is shown in Table 4.

Exposure by Inhalation

Consumer inhalation exposure to NTA can be expected during use of powdered laundry detergents for washing clothes (and general cleaning) and during use of powdered dishwashing detergent products.

Home Laundry Operations--

The airborne concentrations of detergent expected around a laundry site have been determined by Procter and Gamble Corporation (Hendricks, 1970) and Colgate-Palmolive (Hudson, 1978). From these data, the expected airborne NTA concentrations can be calculated if NTA were used in similar formulations of powdered laundry detergents.

In-home dust collection studies were conducted using a cyclic air sampling device and an electrostatic precipitator during typical consumer use (Hendricks, 1970). The average dust inhalation for an average female was experimentally measured to be 0.27 µg/cup of detergent product used. This figure is based on an adult female inhalation rate of 16.3 liters/min and the double-pour method which is the most common method of dispensing powdered detergent. (The double-pour method involves pouring the product from the carton into a measuring aid and then into the washing machine.) The double-pour method generates more dust than any other method for use of a laundry product in the home (Hendricks, 1970). Consumer usage of laundry detergent was calculated; the average (median) amount used per week is 7.8 cups, and at the upper 95th percentile the figure is 22.5 cups/week. The industry-wide average concentration of NTA in powdered laundry detergents sold in Canada is approximately 15% by weight; the maximum amount that is being used in Canada is 25%.

TABLE 4. POTENTIAL EXPOSURE TO NTA FROM CONSUMER USE OF DETERGENT PRODUCTS

Exposure route	Operation ^{a/}	Subject	Exposure (μg NTA/day)	Remarks
Inhalation	Automatic clothes washer	Male adult	0.131-0.378	
		Female adult	0.073-0.217	
	Automatic dishwashing	Child	0.067-0.193	
		Male adult	0.019-0.118	
		Female adult	0.011-0.068	
Percutaneous	Hand dishwashing Hand laundry Residue on clothes	Child	0.010-0.063	
		Adult	8.75-17.5	0.3-0.75 g/l NTA (same as hand dishwashing)
		Adult	1.28	0.01 $\mu\text{g}/\text{cm}^2$ NTA on fabric
		Adult	0.44	
		Child	968	No rinse
Ingestion	Hand dishwashing	Child	968	
		Adult	4.84	Rinse, towel dry
	Automatic dishwasher	Child	4.84	
		Adult	4.84-968	Same range as for hand dishwashing
		Child	4.84-968	

^{a/} Assumes that only NTA-containing products are in use.

For calculations of consumer exposure, NTA is assumed to be homogeneously distributed throughout all size granules; however, NTA may be preferentially associated with the larger or smaller sized particles. Studies to determine the respirability of detergent dust were not available; consequently, in the estimated exposure to NTA in powdered detergents, exposure to both the respirable and nonrespirable fractions of detergent dust is assumed.

The following is the calculated consumer exposure to NTA via inhalation (Winters, 1978a; MRI calculations) expressed as micrograms of Na₂NTA per kilogram per day.

User	Median	95th	$\mu\text{g NTA/day}$
		Percentile	
Female adult (54 kg)	0.001	0.006	0.075-0.217
Male adult (70 kg)	0.002	0.005	0.131-0.378
Child (10 kg)	0.007	0.019	0.067-0.193

These data were calculated based on the following formula:

$$\frac{(\text{detergent dust/cup})(\% \text{ NTA in detergent})(\text{weekly detergent use}) \times (\text{week/day})}{(\text{body weight})}$$

The data used in the calculations are presented below:

- 0.27 μg detergent dust exposure per cup for an adult female, measured in simulated home use, based on an average inhalation rate of 16.3 liters/min (Hendricks, 1970).
- 0.47 μg detergent dust exposure per cup for an adult male, based on simulated home use by Hendricks (1970) and an average inhalation rate of 28.6 liters/min (Biology Data Book, 1974).
- 0.24 μg detergent dust exposure per cup for a 10-year-old child, based on simulated home use by Hendricks (1970) and an average inhalation rate of 14.4 liters/min (Chemical Rubber Company, 1969).
- % of NTA in dust--25% - assumes 25% NTA in detergent with even distribution.
- detergent use--7.8 cups/week - median (Hendricks, 1970); and
--22.5 cups/week - 95th percentile (Hendricks, 1970).

Note: Includes other uses such as presoaking, floor washing, etc.

- median (typical) detergent use - the calculations were made as follows:

$$\text{Adult female } \frac{0.27 \mu\text{g/cup} \times 0.25 \times 7.8 \text{ cups/week} \times 1/7 \text{ day/week}}{56 \text{ kg}} = 0.001$$

$\mu\text{g/kg/day}$

$$\text{Adult male } \frac{0.47 \mu\text{g/cup} \times 0.25 \times 7.8 \text{ cups/week} \times 1/7 \text{ day/week}}{70 \text{ kg}} = 0.002$$

$\mu\text{g/kg/day}$

$$\text{Child } \frac{0.24 \mu\text{g/cup} \times 0.25 \times 7.8 \text{ cups/week} \times 1/7 \text{ day/week}}{10 \text{ kg}} = 0.006$$

$\mu\text{g/kg/day}$

- 95th percentile (extreme) detergent use:

$$\text{Adult female } \frac{0.27 \mu\text{g/cup} \times 0.25 \times 22.5 \text{ cups/week} \times 1/7 \text{ day/week}}{56 \text{ kg}} =$$

$0.004 \mu\text{g/kg/day}$

$$\text{Adult male } \frac{0.47 \mu\text{g/cup} \times 0.25 \times 22.5 \text{ cups/week} \times 1/7 \text{ day/week}}{70 \text{ kg}} =$$

$0.005 \mu\text{g/kg/day}$

$$\text{Child } \frac{0.24 \mu\text{g/cup} \times 0.25 \times 22.5 \text{ cups/week} \times 1/7 \text{ day/week}}{10 \text{ kg}} = 0.02 \mu\text{g/kg/day}$$

Notes: These exposure estimates assume that all of the measured detergent dust is inhaled, that all of the detergent dust is respirable, and that all of the inhaled dust remains in the body. This is not expected in actual practice.

The Colgate-Palmolive Company developed a test in 1970 to measure the amount of dust created from the use of several of its products. The test was designed to simulate the use of automatic washing machines. The actual test consisted of four people standing around a bucket 16 in. in diameter and 33 in. above the floor to simulate a washing machine. Each person poured powdered laundry detergent from a 49-oz box into a cup and the cup was emptied into the bucket. This was repeated until the boxes were empty. An air sampler was situated in an area which would be occupied by a fifth person around the bucket. The sampling was performed during the pouring of the detergents and for various time intervals after the pouring was complete (Hudson, 1978). The results of this study are presented in Table 5.

TABLE 5. DUST LEVELS FROM POWDERED DETERGENTS

Product No.	Total pouring time for 49 oz (min)	Total sampling time (min)	Total amount of dust collected ($\mu\text{g}/\text{m}^3$ of air)	Calculated amount of dust created by 1-1/4 cup over the sampling period ($\mu\text{g}/\text{m}^3$)
1	2	50	1,400	93
2	2	100	2,000	133
3	2	124	300	20
4	2	126	300	20
5	2	200	800	53

Source: Hudson (1978).

Ninety-five percent of detergent dust settles in 100 sec, virtually all detergent dust settles within 2 min (Wendricks, 1970). This information is based on a study using a laser dust detection device developed for this study.

Assuming the breathing rates used in the Procter and Gamble study and an average breathing time of 2 min, the extent of exposure to the levels generated in the Colgate tests were estimated (Table 6). These values, which utilize dust concentrations determined by the Colgate-Palmolive Company, are within the range of exposures calculated in the Procter and Gamble study.

TABLE 6. INHALATION EXPOSURE TO NTA-CONTAINING POWDERED DETERGENT

Detergent product No.	For adult female ^{a/} ($\mu\text{g/kg}$)	For adult male ^{a/} ($\mu\text{g/kg}$)
1	0.014	0.019
2	0.020	0.027
3	0.003	0.004
4	0.003	0.004
5	0.008	0.011

Source: HRI calculations.

^{a/} Calculated as follows: breathing rate (16.3 liters/min, female; 28.6 liters/min, male) $\times$ exposure time (2 min) $\times$ dust concentration ($\mu\text{g/liter}$ (Table 5) $\times 1 \text{ m}^3/1,000 \text{ liters}$) $\times$ maximum NTA content of detergent ($0.25 \div \text{average body weight}$ (54 kg, female; 70 kg male) = estimate.

Automatic Dishwashing Operations--

The potential inhalation exposure to NTA associated with automatic dishwasher detergent use has not been studied. However, inhalation exposure from its use in an automatic dishwasher detergent is assumed to be similar to exposure estimated for laundry detergent (HRI estimate). Two differences should be noted: (a) the dishwashing detergent is poured directly from the box to the dishwasher and is not double-poured as with laundry operations; and (b) the average quantity of dishwashing detergent employed per load [2.5 tablespoons (0.16 cup) versus 1 cup] is considerably smaller. On a per cup basis (assuming a daily consumer use of 1 cup/day maximum; HRI estimate), the detergent dust exposure would be 0.27 μg for an adult female, 0.47 μg for an adult male, and 0.25 μg for a child, resulting in potential NTA exposures of 0.0002, 0.0006, and 0.0006 $\mu\text{g/kg/day}$, respectively. For an average per load usage of 0.16 cup, these maximum values should be reduced by a factor of about 6.25. These data were based on the following formula:

$$\frac{(\text{detergent dust exposure/cup})(\% \text{ NTA in detergent})(1 \text{ cup/day})}{(\text{body weight})}$$

The maximum percentage of NTA that is currently being employed in Canada for granular laundry detergents is 25%. That percentage has been assumed for these calculations.

Exposure by Percutaneous Absorption

Percutaneous exposure can result from (a) contact with washwater during dishwashing, hand and machine laundry operations, and general cleaning with a detergent containing NTA, (b) contact during laundry machine operation, and (c) contact resulting from wearing clothes which have been washed in a detergent containing NTA.

Hand Laundry and Dishwashing--

The following calculation summarizes exposure to NTA if it were added to laundry detergent or light duty detergent (liquid or powdered) and used to wash dishes or laundry by hand (Winters, 1978a).

- calculation

$$\frac{(24 \text{ hr absorption}) \times (\text{skin area}) \times (\text{exposure time})}{(\text{body weight})}$$

- data

24-hr absorption $0.25 \mu\text{g}/\text{cm}^2/\text{day}$ --highest measured for animal skin exposed for 24 hr to a solution of NTA and linear alkylbenzene sulfonate (LAS), each present 0.2% (wt/vol).^{a/}

Note: A typical concentration for doing dishes or laundry by hand would be 0.2 to 0.3% (wt/vol) detergent and the typical NTA concentration in the wash water for doing dishes (and laundry) by hand is 0.050% (0.5 g/liter) to 0.075% (0.75 g/liter), assuming an NTA level of 25% in the product (Winters, 1978c). This concentration is about two times the concentration used in automatic laundry machines (Hopping, 1978a; Winters, 1978c).

^{a/} A study was conducted in 1974 (Hopping, 1979) to determine the skin absorption potential of NTA. The experiment consisted of a single application of carbon-14 labeled NTA and LAS (each present at 0.2%) to the shaved skin of two rats. The animals were restrained for 72 hr and the urine and feces collected. The results showed a maximum 24-hr absorption of $0.25 \mu\text{g}/\text{cm}^2$ for NTA.

Rat skin does not provide a simulation of human skin and is not commonly used for this purpose. Shaved rat skin generally permits greater penetration of chemicals than occurs through human skin so that the absorption rate is probably greater than that which would occur through human skin under normal conditions. Additional tests would need to be performed on other animal skin models before a more precise approximation of human skin absorption can be assumed (Herndon, 1979). However, the calculated exposure given here probably represent an upper limit for the above reasons.

- exposure time--1 hr/day--95th percentile, is 3.85 washes/day at about 15 min/wash; 0.5 hr/day--median, is about 2 washes/day at about 15 min/wash (Hendricks, 1970).

- exposure area--1,680 cm² hand and forearm area for 70 kg adult (Winters, 1978a).

$$1 \text{ hr/day exposure } \frac{0.25 \text{ } \mu\text{g/cm}^2/\text{day} \times 1,680 \text{ cm}^2 \times 1 \text{ hr}/24 \text{ hr}}{70 \text{ kg}} = 0.25 \text{ } \mu\text{g/kg/day}$$

$$0.5 \text{ hr/day exposure } \frac{0.25 \text{ } \mu\text{g/cm}^2/\text{day} \times 1,680 \text{ cm}^2 \times 0.5 \text{ hr}/24 \text{ hr}}{70 \text{ kg}} = 0.13 \text{ } \mu\text{g/kg/day}$$

Note: Absorption flux used was measured at an NTA concentration higher than that which would be found in actual practice. The calculations also assume that absorption for human skin is the same as that for the animal skin.

No data have been found concerning the exposure which could occur if concentrated solutions of detergent containing NTA came in contact with the skin. Similarly, skin absorption from contact with NTA products (laundry or dishwashing) in the powdered form has not been studied. The number of people exposed in this manner would be very large (all persons who handle boxes of detergents), but the contact time would probably be short compared to contact with dishwater. (Most people would rinse their hands shortly after contact with powdered detergent.) The percutaneous data provided by Procter and Gamble (Winters, 1978a) indicate that a 70 kg adult would be exposed to only 0.13 to 0.25 $\mu\text{g/kg}$ of NTA per day resulting from exposure to dishwater containing a concentration of 0.2% (wt/vol) (2.0 g/liter) NTA. However, exposure of the dishwasher or launderer to detergent adhering to the container (or other sources of contact with the powder, such as spills) possibly results in a situation where a fairly highly concentrated solution of the detergent would be in contact with the skin (of the hands, particularly). No data are available to predict the percutaneous absorption rate of higher concentrations of NTA.

Laundry Machine Operations--

The NTA concentration expected in laundry machine washwater is 0.36 g/liter (0.036% wt/vol). This figure was calculated from the following data (Winters, 1978c; Hopping, 1978a).

- 1.25 cups detergent
- 77 g of detergent per cup
- 25% NTA
- 17.5 gal. wash solution volume

Contact with laundry machine washwater does not occur frequently, and when contact occurs it is usually of short duration. (Most people would rinse their hands following such contact.) Because of the infrequent and short duration contact time, no exposure level calculations were performed.

Residue in Clothes--

The extent of consumer exposure to NTA in clothes has been estimated by Procter and Gamble (Winters, 1978a; Hopping, 1978b; Hopping, 1979) using the following method:

$$\frac{(\text{conc. on fabric}) \times (\text{skin area exposed to fabric}) \times (\text{absorption efficiency})}{\text{body weight}}$$

The data employed were:

- concentration on fabric of $0.01 \mu\text{g}/\text{cm}^2$; measured value for fabric laundered in NTA detergent.
- skin area exposed, assume complete coverage 24 hr/day: adult, $1.6 \times 10^4 \text{ cm}^2$ (70 kg); child, $5.5 \times 10^3 \text{ cm}^2$ (20 kg)
- absorption efficiency, 0.8%--highest measured for animal skin exposed *in vivo* for 24 hr to a solution of NTA and LAS, each present at 0.2% (wt/vol). The average NTA concentration in automatic laundry machine washwater is 0.036% (wt/vol), assuming 25% NTA in the detergent.

Note: A typical product use would be about 0.12% (wt/vol) of powdered laundry detergent [i.e., 0.03% NTA (wt/vol)].

The estimated exposures are:

$$\text{Adult } \frac{0.01 \mu\text{g}/\text{cm}^2 \times 1.6 \times 10^4 \text{ cm}^2/\text{day} \times 0.008}{70 \text{ kg}} = 0.018 \mu\text{g}/\text{kg}/\text{day}$$

$$\text{Child } \frac{0.01 \mu\text{g}/\text{cm}^2 \times 5.5 \times 10^3 \text{ cm}^2/\text{day} \times 0.008}{20 \text{ kg}} = 0.022 \mu\text{g}/\text{kg}/\text{day}$$

Note: Not all body skin area is covered with clothes.

Exposure by Ingestion

This section describes potential exposure to NTA via ingestion if NTA were formulated into dishwashing detergents. To the best of our knowledge, NTA is not currently used in the United States or Canadian dishwashing detergents in either automatic dishwashing formulations or in light duty detergents (those intended for hand dishwashing).

Residues Resulting From Hand Washing of Dishes--

One percent of households doing dishes by hand do not rinse their dishes (industry source, 1978). The following calculations summarize NTA exposure from residue on dinnerware resulting from washing dishes by hand and applies to both rinsed and nonrinsed dishes (Winters, 1978a). In these calculations, it has been assumed that all households (76×10^6) will, at sometime, wash dishes or kitchen utensils by hand.

- calculation method

$(\text{deposition on dinnerware}) \times (\text{area of dinnerware use}) \times (\% \text{ of area in contact with food})$
(body weight)

- data

Deposition on dinnerware $0.45 \mu\text{g}/\text{cm}^2$ --measured by chemical analysis for 25% NTA laundry product used at 0.2% (wt/vol) for dishwashing (rinsing and towel drying substantially reduces this amount); daily dinnerware area $4,300 \text{ cm}^2/\text{person}$; percentage of dinnerware area in contact with food 50% (or $2,150 \text{ cm}^2$).

- estimated exposure

$$\text{No rinse/drain dry--Adult } \frac{0.45 \mu\text{g}/\text{cm}^2 \times 4,300 \text{ cm}^2 \times 0.50}{70 \text{ kg}} = 13.8 \mu\text{g}/\text{kg}/\text{day}$$

$$\text{--Child } \frac{0.45 \mu\text{g}/\text{cm}^2 \times 4,300 \text{ cm}^2 \times 0.50}{10 \text{ kg}} = 96.8 \mu\text{g}/\text{kg}/\text{day}$$

Rinse/towel dry--

$$\text{Adult } \frac{0.45 \mu\text{g}/\text{cm}^2 \times 4,300 \text{ cm}^2 \times 0.50 \times 0.05 \times 0.10}{70 \text{ kg}} = 0.07 \mu\text{g}/\text{kg}/\text{day}$$

$$\text{Child } \frac{0.45 \mu\text{g}/\text{cm}^2 \times 4,300 \text{ cm}^2 \times 0.50 \times 0.05 \times 0.10}{10 \text{ kg}} = 0.48 \mu\text{g}/\text{kg}/\text{day}$$

Note: Rinsing dilutes concentration of adhering solution by 1/20; hence, 0.05 in equation. Towel drying removes 90% of adhering solution; hence, 0.1 in equation.

- hand dishwashers that do not rinse: One percent of the 74×10^6 households which do dishes at sometime by hand do not rinse; this equals 74×10^4 households doing dishes and not rinsing ($0.01 \times 74 \times 10^6$). Total persons affected, 2.09×10^6 (74×10^4 households $\times$ 2.83 persons/household).

- hand dishwashers who do rinse, followed by towel or drain dry: 99% of hand dishwashers; 75×10^6 households ($0.99 \times 76 \times 10^6$) do dishes by hand, rinse, and towel dry; total persons affected, 212×10^6 (75×10^6 households $\times 2.83$ persons/household).

Residue Resulting From Use of an Automatic Dishwasher--

The concentration of NTA in the wash water of an automatic dishwasher would be the same concentrations as estimated for hand washing of dishes (MRI estimate) with an NTA laundry product, i.e., 0.05% (0.5 g/liter) to 0.075% (0.75 g/liter). This is based on a 0.2 to 0.3% (wt/vol) concentration of detergent in water and an assumed level of 25% NTA in the automatic dishwasher detergent.

The estimated exposure to NTA from residue on dinnerware following washing in an automatic dishwasher for an adult is estimated to be between 13.6 $\mu\text{g/kg/day}$ (the estimated exposure when hand washed dishes are not rinsed) and 0.07 $\mu\text{g/kg/day}$ (exposure when hand washed dishes are rinsed and towel dried) (MRI estimate). For a child the upper and lower limits would be 96.8 and 0.48 $\mu\text{g/kg/day}$. These exposure estimates are most likely high because the hot water rinses of an automatic dishwasher cycle could lead to less residue on dinnerware than hand wash and rinse.

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TECHNICAL REPORT DATA

(Please read instructions on the reverse before completing)

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16. ABSTRACT The current annual production of trisodium nitrilotriacetate in the United States is approximately 70 million pounds. The production of NTA is highly automated and is largely under remote controls; thus, production workers have little potential for exposure. Analysis of air in the workers' breathing zone indicated that the highest exposure area had an average potential exposure of 8.2 mg NTA/day. NTA was not detected in urine samples of production workers (detection limit, 0.5 mg/liter). The number of detergent production workers that would be directly exposed to airborne detergent dust is estimated to be 2,500; typical exposure during detergent formulation is estimated to be 338 µg/NTA/day. Consumer exposure to detergents can result from inhalation of detergent dust, percutaneous absorption from contact with wash water or direct skin contact with the detergent, ingestion of residue on dishes or utensils, and skin contact with residues in clothing. Estimates of the number of consumers potentially exposed (and the extent of exposure) are as follows: automatic clothes washing, 176 million (0.07 to 0.38 µg NTA/day); automatic dishwashing, 33 million (0.011 to 0.12 µg NTA/day); hand dishwashing, 171 million (8.75 to 17.5 µg NTA/day); residue on dinnerware, 40 million (4.8 to 968 µg NTA/day); and general cleaning, 176 million (8.75 to 17.5 µg NTA/day).	
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Mr. MAGUIRE. Mr. Jellinek, in your letter of May 27 you recommend that manufacturers should conduct monitoring and environmental studies to confirm the predictions of low environmental levels of NTA during the initial years of resumed use.

Does EPA have authority under TSCA and other environmental statutes to require manufacturers and processors to conduct the type of in-depth studies that were recommended by Dr. Shapiro in the letter to which I referred earlier?

Mr. JELLINEK. Yes, we do.

Mr. MAGUIRE. Is it your intention to so require?

Mr. JELLINEK. We will if they do not do it voluntarily. I cannot say that we will require every single study. We will make a judgment as to which ones we think should be done. If we judge that they should be done and the industry does not voluntarily agree to do them, then we will require them.

Mr. MAGUIRE. Would that include in-depth studies of the effects of NTA on aquatic ecosystems?

Mr. JELLINEK. As I say, my staff has not recommended to me which precise studies should be done. We are fully prepared to thoroughly consider each of the recommendations of the IJC and make appropriate decisions on which things should be done.

Mr. MAGUIRE. Would you make those decisions under section 4 of TSCA?

Mr. JELLINEK. It is possible under section 4, under section 8, or under section 5.

Mr. MAGUIRE. Or under a functional equivalent thereof?

Mr. JELLINEK. If it is done voluntarily, it might be a functional equivalent thereof.

Mr. MAGUIRE. Does minority counsel have questions?

Ms. WHITNEY. Yes.

Mr. Jellinek, I want to follow up on something that was brought up earlier.

In your letter of May 27 to Procter & Gamble you listed two reasons why EPA decided not to act here. One of them was the risk assessment that you did. The other one was the higher priority demands based upon your limited resources.

The risk assessment was a 2-year undertaking, wasn't it?

Mr. JELLINEK. It covered that calendar time.

Ms. WHITNEY. Can you give the subcommittee some idea of the weight that was given those two considerations when you made your decision?

Mr. JELLINEK. I cannot really characterize the proportional weight. They were both important. However, I think the first step was the low risk. If we had not felt comfortable with the level of risk in terms of whether this is something that we ought to do more work on or something that we should give a high priority to, then we would have written a different letter.

Ms. WHITNEY. Thank you.

Mr. MAGUIRE. How many low risk carcinogens are you prepared to voluntarily put into the environment that do not pose countervailing health benefits, but rather only perhaps this shirt may be a little whiter than that shirt in certain water types of benefits?

I would suggest we are not just engaging in selling soaps here.

Mr. JELLINEK. I understand.

Mr. MAGUIRE. I just wonder how many times you would be prepared to take upon yourself and upon your agency the burden, because that is what it is, of allowing a carcinogen shown to be so in laboratory tests to be put into the environment for reasons other than countervailing benefits for people's lives and health.

Mr. JELLINEK. Believe it or not, I am glad you asked that question. It gives me a chance to point out that each decision in which we are involved is in some way a unique decision. This is not a precedential decision in terms either of the way it was made or in terms of any statement that my office, EPA, or I are making about the risk.

The factors in this risk assessment, in addition to the quantitative assessment which was only one part of it, led us to believe that on balance this was a low risk situation. When I talk about those factors, I talk about the fact that first of all we did a very worst-case analysis in terms of exposure and everything else. We thought about the worst possible situation and a situation which we thought was probably not the likely situation.

Second, on the health side this chemical is not a mutagen. It is not a teratogen. It appears not to be readily absorbed into the body. It is excreted almost totally in urine and feces.

All of these various features of the chemical, in addition to the exposure and in addition to the quantitative risk assessment, went into the decision. It was a weight-of-the-evidence-type decision as to low risk. It was not an automatic application of some arcane statistics.

Mr. MAGUIRE. Are you perfectly comfortable having a billion pounds of this added to the groundwater, even though there might not be benefits that could be calculated other than a marginal benefit?

Mr. JELLINEK. No; I am not comfortable with it.

Mr. MAGUIRE. You are not comfortable with it?

Mr. JELLINEK. I am not comfortable with it. I said that our decision was not one of safety or of comfort. Our decision was that it was low risk and we would not regulate it.

Mr. MAGUIRE. Fine. That was your agency's decision which you took. If you are not comfortable with it, does that mean that you would prefer that it be marketed or would you prefer that it not be marketed?

Mr. JELLINEK. We have not made any decision on that. I am not prepared to make any statement on that.

Mr. MAGUIRE. Thank you for your testimony.

The hearing is concluded.

[Whereupon, at 4:45 p.m., the hearing adjourned.]

APPENDIX A

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

MAY 27 1980

Mr. W. C. Krumrei
Senior Director
Research and Development
Procter & Gamble Company
Ivorydale Technical Center
5299 Spring Grove Avenue
Cincinnati, Ohio 45217

Dear Mr. Krumrei:

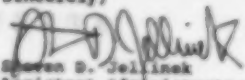
As you have requested, I am writing to inform you of the results of EPA's risk assessment of the use of nitrilotriacetic acid (NTA) in laundry detergents.

Our review, which included all of the major studies generated to date on NTA, finds that the projected levels of exposure from the use of this substance in laundry detergents are generally low and therefore that the associated risks would also be low. Based on these findings and on the higher priority demands upon our limited resources, EPA sees no reason to take regulatory action against the resumed production and use of this substance for laundry detergents. EPA does have a number of recommendations for companies manufacturing and processing NTA to follow. Specifically:

- manufacturers and processors should employ strict controls to limit occupational exposures to NTA.
- NTA should not be used in shampoos, foods, hand dishwashing detergents, and other consumer products designed to have direct dermal or oral exposures
- manufacturers should conduct monitoring and environmental studies to confirm the predictions of low environmental levels during the initial years of resumed use. EPA would like to review the design of such studies.
- and that manufacturers and processors should maintain records of reported ingestions involving NTA-containing detergents.

Warren Muir, Deputy Assistant Administrator for Testing and Evaluation, is available to discuss our findings on any details concerning these recommendations.

Sincerely,


Steven D. Jellinek
Assistant Administrator
for Pesticides and
Toxic Substances

Attachment

cc: Mr. Monte Throdahl, Monsanto

APPENDIX B

FINAL REPORT: NTA

APRIL 22, 1966

(301)

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Appendix A - Conclusions of Selected
Committee ReportsAppendix B - Inhalation Toxicity. Letter
from Procter and Gamble.
June 25, 1979.

PREFACE

This NTA assessment is intended to brief the Assistant Administrator of the Office of Pesticides and Toxic Substances about the current scientific thought concerning the risk to health and the environment posed by the possible use of NTA in detergents marketed in the United States. The purpose of the assessment is to provide a preliminary scientific judgment on which to base an EPA/OPTS policy decision regarding NTA. It is not our intent to duplicate the existing extensive literature reviews on NTA, nor to validate the literature on which those reviews were based. We will assess the risks from NTA but not produce a detailed risk benefit analysis normally required for regulation under TSCA. It is expected that a more rigorous review and assessment would be necessary prior to making a regulatory decision.

Quantitative (where possible) and qualitative assessments of risk to human health and the environment are provided but no attempt is made in this report to determine the acceptability of these risks to the Agency or society. Only the potential risks arising from the detergent use of NTA are examined in this assessment. Human health risk is based on potential exposure via drinking water, industrial and consumer contact. The report includes some recommendations for additional study but does not suggest or recommend specific regulatory options. Neither does it compare the risks of using NTA with the risks of using other detergent builders.

The approach of this evaluation has been to review the findings and recommendations of the major committees that have examined NTA in the last decade, and to supplement them with the most recent information, as necessary. A complete listing of the committee reports and reviews used can be found in the References section. They include reports prepared by the U.S. Department of Health, Education, and Welfare, the International Joint Commission, Environment Canada, and the National Toxicology Program.

Executive Summary

NTA (nitrilotriacetic acid) is an effective substitute for phosphates in building laundry detergents, and has been used for this purpose in Canada since 1973. The Office of Testing and Evaluation has made a review of current information on the health and environmental risk that this use of NTA might present. This report is the result of that review.

NTA production for use in heavy duty laundry detergents alone could reach 1 billion pounds per year; almost all of this would be released into the aquatic environment. In contrast, about 60 million pounds per year of NTA is now used in detergents in Canada.

NTA is rapidly degraded under aerobic conditions at temperatures above 5°C; the biodegradation of NTA does not lead to the formation of persistent intermediates. NTA can be decomposed in sunlit waters by photolysis, and the products of this decomposition are rapidly biodegradable. NTA does not appear to solubilize metals from soils or to facilitate metal transport. In fact, the evidence suggests NTA increases adsorption of heavy metals by soils. Questions relating to the degradation of NTA in anaerobic and saline environments, as well as its behavior at extremes of environmental pH and its relationship to metals in sewage sludge and sediments remain. In addition, the significance and form of the low levels of NTA that appear to be persisting in the Canadian environment require more study.

Small numbers of people (less than 3000 total) would be exposed to NTA during its manufacture and formulation, but virtually the entire U.S. population has the potential for continuous low level exposure in drinking water and consumer detergent products. Long term and extensive Canadian monitoring data show that very low concentrations (national mean = 2.82 µg/l; range from 0.2 to 24.5 µg/l) of NTA are found in drinking water. Similar levels are expected in the U.S. Estimated consumer exposure, too, is low, amounting to daily exposure of less than 1 µg/kg for most adults. Worker exposure, though typically low, can be significant for the few working without protective equipment in the dustiest parts of the operation.

Oral, inhalation and dermal absorption of NTA is relatively poor in man, biotransformation is not measurable, and excretion is rapid. Because of the low acute and subchronic toxicity, NTA or its metabolites are not a high risk at expected exposure levels. NTA is not mutagenic and even in

the presence of heavy metals does not cause teratogenic or reproductive effects. NTA has been shown to produce tumors in the kidneys and urinary tracts of both rats and mice exposed to very high dietary levels. A conservative quantitative risk assessment estimates the oncogenic risk for the general population exposed through drinking water at 1 in 500,000. Exposure and oncogenic risks for detergent formulators are much higher, 1 in 4,000, although ways to greatly reduce exposure in an occupational setting are available. These risk estimates are based on the belief that the tumors that occur at high dose levels would also occur at low exposure levels. The significant body of data presented by the Procter and Gamble Company suggests but does not prove that a threshold for NTA carcinogenicity exists.

Numerous studies on the acute and chronic effects of NTA on aquatic animals have generally demonstrated a low toxicity. Algal growth studies are conflicting, but NTA is not expected to significantly increase nitrogen loadings to surface waters or contribute to eutrophication problems. No obvious environmental problems have surfaced during the use of NTA in Canada over the last decade. At the low expected environmental concentrations (similar to those in Canada), no adverse environmental effects are anticipated, but confirmatory monitoring or testing under realistic conditions is needed.

I. Introduction

NTA (nitrilotriacetic acid) is a triprotic acid with the following chemical formula: $N(CH_2COOH)_3$. The trisodium salt of this acid is used as a detergent builder, and use in detergent formulations is by far the greatest potential application of the product. NTA is desirable in detergents and other products because of its ability to sequester (form soluble complexes with) calcium and magnesium ions.

NTA became important in the detergent industry in the late 1960's primarily because a replacement was needed for sodium tripolyphosphate, the predominant detergent builder at the time. Detergent phosphates had come under scrutiny as the principal and most controllable cause of eutrophication problems in lakes. Anticipating public and legislative pressure to reduce the phosphorus content of detergents, detergent manufacturers and suppliers geared up for the large scale production of NTA.

In late 1970, preliminary findings from a study conducted at the National Institute of Environmental Health Sciences (NIEHS) suggested that NTA might increase the teratogenic activity of methylmercury. Based on these preliminary findings, the major detergent manufacturers and suppliers agreed, at the request of the Surgeon General, to discontinue the use of NTA pending further study.

The concerns raised by this study were refuted by subsequent review and testing efforts by the industry, the U.S. Government, and task forces of the International Joint Commission (IJC), a joint Canadian-U.S. advisory group concerned with the water quality of the Great Lakes.

The first of these reviews was prepared by Arthur D. Little, Inc. (ADL) in 1971 for the Proctor and Gamble Company. The report held that NTA did not appear to present a carcinogenic hazard to man, but recommended that additional studies in two species be initiated. In the opinion of ADL, a series of controlled experiments had been performed which alleviated the concerns raised in the initial NIEHS report linking NTA and heavy metals with fetal toxicity and teratogenic activity. The report also indicated that additional short term experiments should be conducted on the influence of NTA in such areas as toxic metals effects on genetic material. The report concluded that approval for the use of NTA in detergents should be coupled with an environmental monitoring program and continuing research on environmental and human safety.

In April 1972, an ad hoc committee (the "Woods Committee") was formed by the Assistant Secretary for Health and Scientific Affairs of the Department of Health, Education and Welfare (DHEW) to examine all relevant health and safety information on NTA. In their final report, the group stated that "NTA is not likely to be toxic to man at levels expected in daily use," but expressed reservations concerning the carcinogenic and mutagenic risk of NTA. Additional studies were recommended to clarify both of these areas. The Woods committee also recommended that if NTA were permitted in detergents, the NTA content of detergents should be noted on the package label and a monitoring system should be established to measure NTA and nitrogen levels in ground and surface waters; NTA levels in freshwater fish, fish-eating birds and human bone; zinc levels in human bone; and the incidence of human degenerative renal disease. They also recommended epidemiologic studies of populations exposed to high levels of NTA. Additional details of the Woods committee's recommendations can be found in Appendix A.

In August 1974, following a request from the Office of the Secretary, DHEW, an NTA subcommittee of the DHEW Committee to Coordinate Toxicology and Related Programs was formed. This subcommittee was formed at that time to evaluate a long term study of Na₂-NTA in the drinking water of rats. The study was conducted by Dr. Robert Goyer at NIEHS. The greatest cause of concern was a statistically significant increase in renal adenomas among treated animals that died before terminal sacrifice. The incidence of severe renal tubular hyperplasia was significantly increased among treated animals. The subcommittee concluded that the available evidence indicated a carcinogenic effect of NTA on the urinary tract in rats under the conditions of the test.

During the early 1970s, phosphorus induced eutrophication problems became widely recognized; they were especially critical in the Great Lakes area. Canada, and some States and municipalities in the U.S., moved to ban or limit the phosphorus content of detergents. The national policy of EPA was to control phosphorus by incorporating phosphate removal processes in wastewater treatment plants. In Canada, where only 2.2% phosphorus is allowed in detergents, no steps have been taken to restrict the 60 million pounds of NTA used each year but drinking water standards have been set at 50ppb. In areas in the U.S. where phosphorus has been banned or limited, carbonate, silicate or citrate built detergents are currently in use, and other builders, e.g., carboxymethyloxysuccinate (CMOS) and zeolites, are being developed and test marketed. In areas where phosphates are not banned, phosphorus levels average 7.4% (Whelan, 1978).

Within the IJC, a movement to ban phosphates in detergents persisted. All of the Great Lakes states except Illinois have limited or are considering limiting detergent phosphorus to 0.5%. At the same time, concern was raised in the IJC about the replacements for phosphates, and task forces were formed to look at the health and environmental effects of NTA and other nonphosphate builders.

An IJC Task Force on the Health Implications of NTA, chaired by Paul Foley, made the following conclusions in their report issued in May 1977:

1. That available data on NTA and its salts do not indicate potential teratogenicity or mutagenicity.
2. That the only evidence of possible concern to the general population and workers exposed to NTA is the study which showed cancers of the urinary tract in rats and mice given large doses of NTA over their lifetimes.
3. Calculating from the animal data, the maximum probability of tumor formation in rodents at levels of NTA to which humans are exposed is generally within an order of magnitude of 1 in 2 million.
4. In considering what these estimates might mean in terms of cancer risk to man, one must take into account: (a) that the rodent probabilities are exaggerated, and (b) that human absorption of NTA from food or water is about one-fifth of the degree of absorption demonstrated in rats.

More details on the task force report are contained in Appendix A.

The IJC Task Force on the Environmental Effects of NTA, chaired by Joseph Shapiro, completed its findings in late 1978. This task force took a critical look at NTA with particular reference to adverse environmental effects, choosing not to repeat the general reviews of NTA that were available. The task force reached the conclusion that there is nothing in the literature or from the Canadian experience to indicate that the use of NTA would constitute an obvious environmental hazard. The members did, however, express concern over certain gaps in knowledge of the environmental behavior and effects of NTA. They, therefore, recommended that NTA not be prohibited from use as a detergent builder, but that use be accompanied by studies to address specific questions in these areas (see Chapter VI and Appendix A).

In May, 1979, the National Toxicology Program appointed a subcommittee to review and critique a statement submitted by the Procter and Gamble Company concerning the mechanism of NTA carcinogenicity. The statement described various physiological effects that preceded or accompany the appearance of NTA related tumors and suggested that they, rather than NTA itself, are responsible for the induction of the tumors. The NTP subcommittee concluded from its review that the mechanism of NTA carcinogenesis and the threshold level of exposure, if there is one, remain unknown. They also estimated using linear extrapolation techniques that the maximum potential urinary tract tumor risk in rodents at an average drinking water exposure level (0.07 ug/kg/day) to be 2×10^{-6} .

II. Production and Uses

The annual production of NTA in the United States is currently 70-75 million pounds. At the present time, most of this (60-65 million pounds) is exported to Canada and Europe for use as a detergent builder (Task Force Report, 1977). The remaining 10-15 million pounds is used domestically in a variety of applications including industrial water treatment (5.6 million pounds), metal cleaning (.6 million pounds), institutional cleansers (1.6 million pounds), textile preparation (1.2 million pounds) and other miscellaneous uses (.8 million pounds) including use as a builder in some minor brands of U.S. detergents (industrial source).

Existing and potential uses of NTA are listed in Table 1. NTA is and has the potential to become incorporated into many diverse uses because of its chelating abilities; some of these uses are associated with widespread environmental release and/or human exposure. EDTA (ethylenediaminetetraacetic acid) is currently used in a number of these applications, and although EDTA is a more powerful chelator than NTA, it is possible, although unlikely, that EDTA could be replaced by NTA if market conditions permit.

NTA is currently produced in the United States by only two companies, Monsanto and W. R. Grace. The combined capacity of the Monsanto plant near Alvin, Texas and the W. R. Grace plant at Nashua, New Hampshire is 125 million pounds (Centofanti, 1978). These plants are not currently operating at capacity, and if NTA were used in detergents sold in the United States, an additional 50 million pounds of NTA could be ready for the detergent market in a short time (assuming the uses for current production were not changed).

Table 2 shows projected production levels of NTA for use in heavy duty detergents by 1982, with a possible maximum of over 1 billion pounds of NTA for this use alone (this is based on a 25% NTA content in all such detergents). These figures are derived from the current experience in Canada where the industry-wide average NTA content is 15% by weight and the maximum NTA content in detergent formulations is 25% by weight. However, these figures are probably higher than would be true in the U.S., because the detergent industry appears to be moving away from dependence on just one detergent builder. Many alternative builders are in use now and are being developed to accommodate varying water hardness conditions across the country and local restrictions on the use of sodium tripolyphosphate.

The Canadian experience is based on the fact that a limitation of 2.2% phosphorus in detergents has been in effect since 1973. Similar nationwide phosphorus legislation is unlikely in the United States; hence the most

Table 1. Existing¹(*) and Potential² Applications for WTA

A. Industrial Applications

Stabilization of foam
 Maintenance of clarity of shampoos and liquid soap products
 Photographic development
 Stabilization of polymers and plastics against heat deterioration
 Manufacturing of inorganic chemicals
 *Water softening for textile treatment and dye stabilization
 *Detergent builder (including industrial & institutional cleaners)
 *Metal plating and cleaning
 *Industrial water treatment

B. Medicinal and Pharmaceutical Applications

Stabilization of Antisymphilitic compounds
 Stabilization of certain drugs and biological specimens
 Protection against radiation
 Denture cleaners
 Hospital disinfectant¹

C. Agricultural and Food Processing Applications

Complexing of soil nutrients for plant absorption
 (proposed additive to phosphate fertilizer)
 Stabilization of pesticides
 Plant growth regulator
 Prolongation of shelf life of cooked foods
 Treatment of boiler water that, as steam, will be in contact with food

¹ Industrial source.² from Mottola, 1974

Table 2. Estimated 1982 Production Levels of NTA for Use in Heavy Duty Laundry Detergents (millions of pounds).

Total Detergent Sales ¹	Production Factor	Total NTA Used in U.S. (if allowed)	Total NTA Used in Canada ⁴	Total NTA Made in U.S. ⁵
4180-4440	15% ²	627-666	63-67	690-733
	25% ³	1045-1110	63-67	1108-1177

¹ U.S. only. Projection based on annual growth rate for detergents of 1.5-2%. (Whalen, 1978)

² The Canadian experience shows that in a country limited to 2.2% phosphorus in detergents, NTA occupies 15% by weight of the market on an industrywide average.

³ The worst-case scenario, assuming that all laundry detergents in use contain 25% NTA, the maximum seen in Canadian detergent formulations.

⁴ Assuming the Canadian detergent market grows at the same rate as the U.S. detergent market (1.5-2% per year) and average NTA content remains 15% (i.e., phosphorus limitation remains at 2.2%).

⁵ Assuming the Canadian detergent formulators continue to buy NTA from the U.S. at present rates.

promising market for NTA-built detergents is in areas where phosphorus is currently banned or limited, which constitute 20-25% of the total detergent market (Whelan, 1978). It is expected that if NTA were available it would receive immediate application in laundry detergents in these areas (e.g., the Great Lakes region). In addition, other areas might initiate action to ban or limit phosphates if NTA becomes available since it is an acceptably effective phosphate substitute. Phosphorus reduction in detergents may have a positive effect on some waters that receive a high percentage of phosphorus loading from sewage and help reduce the costs associated with nutrient removal at sewage treatment plants.

In addition to its use in heavy duty laundry detergents, NTA has the potential for use in automatic dishwashing detergents, light duty (hand dishwashing) detergents, other soap and shampoo products, and as a replacement for EDTA in some uses. No data were available to make production projections in these areas, but these other uses could raise the total production figure for NTA significantly.

The situation in foreign countries is varied. Finland, Sweden, the Netherlands and Norway use NTA and the latter two countries have set drinking water standards at 50 ppb. Sporadic use has occurred in Peru, the Philippines, and Venezuela. Australia is reviewing the potential health hazard. Germany has no regulations prohibiting NTA use but it is possible that phosphate reduction programs under study could result in NTA use. NTA has been withdrawn from the Japanese market by the manufacturers (National Toxicology Program, 1980).

The predominant uses projected for NTA at this time, in detergents and soap products, are associated with a high degree of environmental release. It is reasonable to assume that virtually all of the NTA in detergent products would enter private or public treatment systems by way of household wastewaters, meaning that more than 1 billion pounds of NTA could be released annually to the environment.

Environmental release during manufacture has been more difficult to determine. No monitoring of effluents or emissions from manufacturing or formulating facilities has been reported, but the processes are such that fugitive dust emissions are probably the principal source of any NTA lost during manufacture or formulation (Midwest Research Institute, 1979). It can be assumed that NTA release resulting from use as a detergent builder would be far greater than release during manufacture.

III. Environmental Fate and Concentrations

The material in this chapter is based on several major reviews by industry, Environment Canada, and a Task Force of the International Joint Commission. While these reviews contain some material which must be accepted with reservations, the evidence discussed in these reviews and in the literature cited does lead to the following conclusions:

- NTA is rapidly and completely degraded under aerobic conditions at temperatures above 5°C.
- The biodegradation of NTA does not lead to the formation of persistent intermediates.
- NTA can be decomposed, in sunlight waters, by photolysis, and the products of this decomposition are rapidly biodegradable.
- NTA does not appear to solubilize metals in soils and facilitate metal transport. In fact, the evidence suggests NTA enhances adsorption of heavy metals by soils.

A detailed discussion of studies on the environmental fate of NTA follows.

The utility of NTA in detergent formulations lies in its ability to form water soluble complexes with calcium and magnesium ions. The trisodium salt of this acid is used as a detergent builder. The commercial sodium salt is a white powder with a purity of 99.4 and a water solubility at 25°C of 49% by weight. Impurities include HCN, NaOH, Na_2CO_3 and primary and secondary amines.

NTA also may form complexes or chelates with other cations and it forms 1:1 complexes with most metals. The latter property is the most significant aspect of its chemistry with respect to environmental fate. The amount of metal-NTA complex formed depends upon the concentration of metal, the concentration of NTA, and the formation constant for the particular complex (Winters, 1977). The relative strengths of the various metal-NTA complexes can be seen by comparing their stability constants. Such a comparison will not indicate, however, the relative amounts of each complex that would be formed; that is controlled by the stability constant and by the concentration of ions that are in equilibrium with it. In addition, it is the totally deprotonated form of NTA that is effective in chelation, and a large fraction of NTA will exist in the NTA^{3-} form only at high pH values. Thus the reaction of NTA with hydrogen ions

at environmentally common pH values reduces the degree of WTA complexation with metals. A determination of the actual extent of complexation in the environment is further complicated by the fact that most metals form other complexes in the environment, such as hydroxides and carbonates, and the total concentration available for complexing is usually less than the total concentration of each species of metal.

Theoretically, the introduction of WTA to an aqueous environment containing soluble metal ions, precipitated metal salts, or adsorbed metal ions may result in metal complexation with WTA and solubilization of previously insoluble metal. The extent to which this solubilization will occur is very dependent upon the concentration of WTA. Investigations by many workers, some employing metal-rich sediments (Gregor, 1972; Barica et al., 1973; Sanchez and Lee, 1973; Banat et al., 1974; Allen and Boalayangoor, 1977) showed that significant release of metals from the sediments, and subsequent solubilization as the WTA complex, generally occurs only when WTA is present at concentrations of 1 mg/l or higher.

Studies of the photochemical degradation of WTA-metal complexes (Stolsberg and Numa, 1975; Trott et al., 1972; Langford et al., 1973) have suggested that photochemical degradation will occur and that iminodiacetic acid (IDA) may be formed. The IDA that is produced probably degrades rapidly in neutral waters, but its fate in acidic waters is not resolved.

Chlorination of WTA produces IDA, N-Chloro-IDA, and glycine. These products do not accumulate because their reactions with chlorine are even more rapid than those of WTA. The presence of ammonia, as in sewage, reduces WTA chlorination by forming chloramines that do not react with WTA. Divalent metal ions retard the reactions by forming metal-WTA complexes which are not susceptible to oxidation by chlorine.

The analytical method of choice appears to be that developed by Aue et al. (1972) which is based on converting WTA to its tri-n-butyl ester and analyzing the ester by gas chromatography. Malaiyandi et al. (1979) discuss a modification of that method which allows a fivefold to sevenfold increase in sensitivity and allowed detection down to 0.2 ug/l.

Environmental Transport

The water solubilities of NTA and NTA-metal complexes suggest that they will be transported through the environment principally in solution with water. Environmental monitoring tends to confirm that conclusion.

Sorption of NTA to sediments and other particulates is known to occur, but this is not believed to be significant because desorption is equally rapid. Indications are that NTA is not removed from water by chemical precipitation or by adsorption on activated carbon in tertiary waste treatment procedures. However, there remains some uncertainty regarding the sorption of NTA to solids and this is of particular concern in waste treatment where relatively high concentrations of NTA-metal complexes will be found if NTA becomes a major constituent of detergent formulations. Studies carried out by Gledhill (Matheson, 1977) showed only slight adsorption to sewage sludge. Following a 30-minute contact period, and with an initial NTA concentration of 10 mg/l, the maximum adsorption on activated sludge was about 0.24 mg/kg, while the amount on primary sludge was only 0.008 mg/kg. Although these values are low, there is some concern that sorption of NTA-metal complexes on such sludges may ultimately lead to a concentration of NTA-metal complexes in subsequent disposal sites such as landfills or agricultural lands. Because of the heavy metal chelation properties of NTA, the effects of land disposal of sewage sludges on heavy metal concentrations in ground waters and on heavy metal introduction into the food chain through field crops need further study.

The metal solubilizing ability of NTA appears to be more significant than sorption on sludge solids, and most studies (Shannon, 1975; Renn, 1974; Nilsson, 1971; Stoveland et al., 1979) show that metal transport through waste treatment plants can be enhanced by the presence of NTA. This is particularly true when the treatment plant is overloaded or operating at low temperatures or when the microbial population is not adapted to NTA degradation. NTA also interferes with physical/chemical attempts to remove heavy metals from a waste stream by such processes as precipitation with lime or alum (Nilsson, 1971).

Another way by which NTA may enter the environment is via ocean disposal of wastewater and sludges. This is of particular concern because of uncertainties with respect to the biodegradation of NTA in marine and estuarine environments (discussed below).

Biodegradation: General

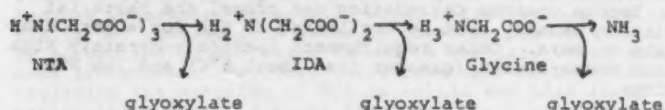
There is considerable evidence from both laboratory studies and field observations that NTA, even when complexed with metals, biodegrades substantially and rapidly in aerobic, nonsaline waters. There is general agreement that the degradation is brought about by acclimated microorganisms and that the end products are CO_2 , H_2O , nitrate or NH_3 . Before optimum degradation can occur, the bacterial population usually must be acclimated to NTA for a period of 2 weeks or more. Other requirements include moderately high ambient temperatures (greater than about 5°C) and low NTA loadings.

Of the various factors affecting biodegradation of NTA in nature, temperature is one of the most significant. Degradation in sewage treatment plants may be 98% complete in summer but significantly reduced in winter (Thayer and Kensler, 1973; Rudd and Hamilton, 1972; Shannon et al., 1974). Un aerated lagoons may freeze over and become anaerobic; under these conditions the removal of NTA is nearly zero.

Relatively little is known about the degradation of NTA under anaerobic conditions. Under strictly anaerobic conditions the biodegradation of most organic materials is slow, and NTA is no exception. Nevertheless, studies have demonstrated that some degradation of NTA takes place under anaerobic conditions such as flooded soils, lake sediments, and septic tanks. However, if significant concentrations of NTA should accumulate in the environment, it is most likely that this will happen in areas of low oxygen concentration, particularly if the temperature also is low.

In NTA monitoring studies in Canada, it was found that at one residence supplied by a well and provided with a septic tank sewage disposal system, the drinking water contained 3.9 mg/l of NTA, while at 20 other similar sampling sites NTA concentration ranged from 10 ug/l to 250 ug/l (Matheson, 1977). At the time of sampling there was apparently waterlogging in the septic bed of the first residence and the anaerobic conditions allowed the NTA to persist and reach the drinking water. Of course, as with similar studies, such a result raises numerous questions about the other contaminants besides NTA that might reach the well water.

There has been concern over the possibility that the degradation of NTA might produce toxic intermediates. Studies using cell-free extracts and metabolic inhibitors (Cripps and Noble, 1973; Tiedje et al., 1973; Firestone and Tiedje, 1978) have shown that the degradation of NTA occurs via carbon-nitrogen cleavage, with the formation of intermediates such as iminodiacetate (IDA), glyoxylate, glycinate, and ammonia, as shown below.



Glyoxylate and glycinate are normal metabolic intermediates of microbial metabolism and are considered innocuous. IDA, however, was postulated by Epstein (1972) to present a potential threat. The theory was that IDA might yield N-nitrosoimino-diacetate (NIDA), a nitrosoamine, and that the NIDA might be carcinogenic to mammalian species. Numerous studies have demonstrated the improbability of IDA accumulation during NTA biodegradation in nature (Cripps and Noble, 1973; Focht and Joseph, 1971; Tiedje et al., 1973; Tiedje and Mason, 1974; Warren and Malec, 1972; Firestone and Tiedje, 1978) and attempts to isolate IDA or NIDA in pure cultures or from river waters or soil have failed. Apparently IDA is a transient metabolite and is biodegraded more rapidly than NTA.

Biodegradation: Waste Treatment Plants

It is now generally accepted that NTA will biodegrade fairly rapidly to innocuous end products in well operated aerobic waste treatment processes. There are several factors which must be recognized as modifying that general statement. The first factor is the substantial period of acclimation required after the introduction of NTA, before the microbial population will achieve the maximum rate of NTA degradation. Acclimation times of 1 to 4 weeks are generally required. Another factor is the influence of temperature on NTA removal in sewage treatment plants. A third factor, which applies equally to any biodegradable constituent of sewage, involves conditions in the treatment plant and if the plant is overloaded or biologically upset (e.g. experiencing sludge bulking or suffering from a pH or toxic agent shock) the NTA degradation will be reduced and more of the chemical will persist to be discharged in the plant effluent. The NTA in wastewaters appears to have no adverse effect on the secondary waste treatment processes.

Activated sludge systems, trickling filters, oxidation ponds and lagoons, all aerobic systems, have been shown to be efficient at removing NTA. Even under winter conditions, degradations in activated sludge and trickling filter can continue at high levels. In a study at Iowa State (Sleasby et al., 1974), more than 90% of the NTA passing through a trickling filter was degraded in warm weather. During the winter months the trickling filter still degraded an average of 82% of the NTA. This is significant because of the short residence time for sewage in a trickling filter. Lagoons and waste stabilization ponds are most susceptible to reduced NTA degradation because of weather extremes. Studies by Rudd and Hamilton (1972) showed significantly reduced NTA removal with decreasing tempera-

Temperature, °C.	15	5	0.5
Average % Removal of NTA:	93	47	22

Biodegradation in anaerobic waste treatment systems is not as certain as under aerobic treatment, but it appears that under strictly anaerobic conditions slow biodegradation can occur (Enfors and Molin, 1973; Moore and Barth, 1974). Moore and Barth's work (1976) suggested that activated sludge containing NTA acclimated organisms transferred to an anaerobic digester (as would happen at many treatment plants), good removal will occur, exceeding 2 mg/l per day. There appears to be a need for further research on these processes since most studies have indicated that NTA degradation is slight in anaerobic digestion and flooded septic tank systems. Septic tanks rarely operate under completely anaerobic conditions and, as noted by Enfors (1974), up to 25% of the NTA can be degraded in a septic tank with a retention time of 2 days.

NTA in Fresh Water

NTA which enters rivers, streams and lakes appears to be slowly biodegraded provided the water is aerobic and not stagnant. As an example, a survey by Shannon et al. (1974) in Ohio found that during the summer, when NTA removal in a treatment system was 95% and water temperature was 20°C, the combined effect of stream dilution and biodegradation gave downstream NTA concentrations consistently below 100 µg/l. On the other hand, during winter, when NTA removal in the treatment plant was 5% and the stream temperature ranged from 0.5 to 3°C, downstream concentrations averaged 106 µg/l. There was evidence that in-stream biodegradation of NTA was continuing, however, even at these low temperatures.

As noted earlier, photochemical decomposition of NTA can occur and in open, sunlit surface waters this process may be an important adjunct to the biodegradation of NTA.

Biodegradation, photochemical decomposition, dilution, and dispersion all combine to make the accumulation of NTA in receiving streams unlikely. The Canadian experience confirms this.

Studies by Dunlap et al. (1971) have shown that NTA can degrade anaerobically in groundwaters, with the conversion of NTA nitrogen into ammonia.

Biodegradation: Marine and Estuarine Waters

The biodegradation of NTA in marine and estuarine waters is a subject of uncertainty and needs much more study. Bourquin and Przybyszewski (1977) and Gledhill and McDonald (1976) were unable to demonstrate NTA degradation by microorganisms isolated from estuaries. However, Borquin and Przybyszewski (1977) found that bacteria from estuarine surface layers were easily adapted to the degradation of NTA in a fresh water medium. Their data indicated an interference with NTA catabolism by some unknown factor of the estuarine environment rather than an absence of potential NTA-degrading bacteria. It has been suggested that the high ionic strength and the chloride ions in such waters may inhibit monooxygenase activity necessary for NTA biodegradation. If this is so, then it is curious that Gledhill and McDonald were able to acclimate marine microorganisms to degrade NTA. In their studies, after about six weeks, marine microorganisms were degrading 97.5% of added NTA while no significant removal of NTA occurred in estuarine systems after 12 weeks of exposure. Monitoring data at Vancouver, B.C., and at Halifax Harbor, N.S. (Prakash, 1976) furthermore, showed no detectable concentrations of NTA. The question of NTA degradation in saline waters needs to be more fully understood, especially before any significant ocean dumping of sewage sludges which may contain undegraded NTA is allowed.

Biodegradation: Soils and Sediments

Soil biodegradation studies by Tiedje and Mason (1974), Dunlap et al. (1971) and Tabatabai and Bremer (1975) have shown that NTA degrades completely in aerobic soils, sometimes after a lag of up to 6 days. Tiedje and Mason (1974) also showed that degradation of NTA would occur at 2°C in

soils with microorganisms acclimated at 12.5°C. These authors also demonstrated that the degradation rates in subsoils were always less than for surface soils from the same site, and that degradation rates did not correlate with pH, drainage, texture, or plant cover. However, as in aqueous systems, microaerobic or anaerobic conditions greatly reduce the rate of NTA degradation. Under waterlogged conditions, simulating flooded percolation fields serving septic tanks, the results suggested that NTA could remain undegraded. Monitoring in Canada has confirmed this possibility.

Relatively few studies have been made with NTA and sediments, but it seems likely that the situation with respect to biodegradation would be similar to that in soils and water, with biodegradation being relatively rapid and complete in the presence of oxygen and with temperatures above 5°C, once the microorganisms have acclimated to the NTA. Studies with NTA and sediments have tended to focus on the possibility that NTA may solubilize toxic metals in such sediments and then release those metals, in a soluble form, as the NTA portion of the complex is degraded. Such studies have shown that the NTA-metal complexes do degrade and the solubilized metal ions do not remain soluble once the NTA portion of the complex has degraded.

Of considerable concern has been the possibility that NTA might complex with soil metals and that the solubilized metal would then be subject to rapid transport in water. Firestone and Tiedje (1975) have noted that both soil and NTA-degrading organisms destabilize the metal-NTA complex. Huang et al. (1977) found that, in the presence of NTA, the adsorption of heavy metals to soil is increased. Sanchez and Lee (1973) found that NTA in lake water reduced the leaching of copper from lake sediments, at the same time enhancing the solubilization of iron and manganese.

Biodegradation: Metal Complexes

As indicated previously, the metal complexing ability of NTA has been the most significant factor of environmental fate concern with respect to NTA. There are conflicting reports concerning the biodegradation of NTA metal complexes, although numerous studies (Firestone and Tiedje, 1975; Shannon, 1975; Dunlap et al., 1971; Forsberg and Lindquist, 1967; Swisher et al., 1967) have been made on the degradation of NTA-metal chelates in a variety of environments. Of the various metal chelates tested, those with Cu, Cd, Ni, Zn and Hg are generally degraded at slower rates than others, such as those with Ca, Mg, Fe and Pb, although the reported studies vary somewhat in their findings. Firestone and

Tiedje (1975), for example, found that the chelates of NTA with Ca, Mn, Mg, Cu, Zn, Cd, Fe, and Na degraded at nearly equal rates, so long as the metal concentrations are low enough to avoid toxicity to the bacteria from the free metal. Firestone and Tiedje also noted that both soil and NTA-degrading organisms will destabilize the metal-NTA complex, which suggests that, in the natural environment, both would act to limit mobilization of metals as soluble NTA chelates.

It appears that biodegradation of NTA-metal complexes will proceed first with the most readily degraded complexes. The most readily degraded complex, apparently, is that with calcium, and since calcium is present at relatively high concentrations in most natural waters, this results in NTA being present to a great extent in a complex in which it is readily biodegradable. At low concentrations of NTA, the complexes which form will depend upon the concentrations of the various metal ions available. It has been speculated (IJC Task Force Report, 1978) that the residual levels of NTA found in Canadian waters may be levels of NTA complexed as its more persistent chelates, those with Cu, Zn and Ni.

Monitoring

NTA has been used in Canada since 1970 as a replacement for phosphates in detergents. Since 1973, when phosphates in laundry detergents were limited to 2.2%, Canadian household detergents have contained an average of 15% by weight of trisodium NTA. A national monitoring and surveillance program was initiated in 1971 and has continued to the present.

The average level of NTA in Canadian wastewater, with NTA comprising 15% by weight of the detergent formulations, on an industry-wide basis, was estimated to be 3.2 mg/l (Brownridge, 1977), based on annual consumption of detergent and per capita consumption of water. Although the level of NTA in sewage plant influents varied from city to city in the Canadian monitoring program, the geometric mean of 3.8 mg/l for measured concentration is very close to the estimate.

For waters beyond the waste treatment plants, monitoring studies (Matheson, 1977; Task Force Report IJC, 1978; Woodiwiss and Walker, 1979) have shown concentrations from <0.2 ug/l to 1 mg/l in receiving waters just below sewage treatment plants and <0.2 to 60 ug/l in drinking water. In a recent report, Malaiyandi et al. (1979) have reported a national mean concentration in raw water, from 70 Canadian municipalities, of 3.88 ug/l, with a range from <0.2 to 33.5 ug/l.

Of 21 private well water samples analyzed 20 samples showed levels at <0.2 ug/l; the remaining sample, from a residence with a waterlogged septic bed, contained 16.9 ug/l NTA. All samples were collected during winter months, from late November 1976 to early February 1977. The important implications of this survey are that the levels of NTA in Canadian waters are not increasing, and that rapid biodegradation of NTA is occurring even at winter temperatures.

As noted earlier, samples of water from Vancouver Harbor, B.C., and from Halifax Harbor, N.S., have contained no detectable concentration of NTA.

The harbor at Hamilton, Ontario, and the western portion of Lake Ontario have been monitored regularly since 1971 for NTA. Most locations in western Lake Ontario have shown NTA concentrations of less than 0.2 ug/l, with a single high value of 162 ug/l in one sample taken near Toronto. Hamilton Harbor has been found to contain detectable NTA at a number of stations, with concentrations as high as 94 ug/l. Circulation patterns, wastewater outfalls, and changing wind conditions appear to be some of the factors which can contribute to localized elevated NTA concentrations, as found at Hamilton.

There are questions about much of the data from the Canadian monitoring studies. Interlaboratory comparisons have not agreed well due to differences in analytical methods, uncertainties about sample preparation, and a lack of replicate sampling. Nevertheless, there seems to be little reason to doubt the overall conclusions from the Canadian monitoring experience. It seems certain that NTA is rapidly and substantially degraded by aerobic waste treatment processes and in aerobic soils and waters. It also appears that NTA concentrations are not increasing in the Canadian environment and that a relatively persistent background level of a few ug/l may be found, possibly due to the complexation of NTA as the more persistent chelates with Cu, Zn or Ni.

Expected Concentrations in U.S. Environments

It has been predicted that if NTA were substituted for phosphates in all household laundry detergents in the United States, as much as one billion pounds would be used annually (see Production and Use, Chapter II). It has been estimated that this could lead to domestic wastewater with as much as 20 mg/l NTA. Estimates by Artman (1973), allowing for

biodegradation and dilution, predict that the receiving waters of the U.S. would contain no more than 25 ug/l NTA. It seems reasonable to assume that, if NTA were substituted for phosphates in U.S. detergents, the environmental concentration would be similar to that observed in Canada, with perhaps some increase in the Great Lakes. These speculations may be off target due to denser populations and differing environmental circumstances in the United States.

In view of the slower degradation of NTA under anaerobic and microaerobic conditions and in consideration of the fact that oxygen is less soluble in warm water than in cold water, it may be that a potential for high NTA concentrations in U.S. waters would exist in warm waters with high organic loadings, such as in southern swamps and in highly polluted streams at summer temperatures (which conditions often coincide with low stream flows and consequent reduced dilution). This is a possibility which will have to be carefully watched if NTA is introduced into the U.S. detergent market.

Additional Research

There are a number of uncertainties with respect to the fate of NTA in the environment. Research should be conducted to resolve as many of these uncertainties as possible, and a vigilant monitoring program should be pursued where NTA is used. Among the questions which need to be answered are the following:

- o Will the use of NTA lead to an increase in metals (especially heavy metals) in sewage sludges, which may be disposed of on agricultural lands or in ocean dumping?
- o Will NTA degrade sufficiently in natural anaerobic environments (e.g. swamps, highly polluted streams) to prevent accumulation?
- o Does NTA degrade in saline waters? Why do laboratory studies show a lack of biodegradation in estuarine waters, but apparent biodegradation occurring in ocean waters?
- o What is the significance of the low levels of NTA which appear to be persisting in some Canadian environments? Are these, as has been speculated, levels of NTA complexed as its more persistent chelates with metals?

- o What concentrations of undegraded NTA will be found in anaerobic digester sludges just prior to disposal as, e.g. in landfills or in ocean dumping?
- o What would be the fate of NTA at extremes of environmental pH, say above pH9 and below pH5?

IV. Human Exposure

If NTA is used widely in U.S. detergents, virtually the entire population will be exposed through drinking water contaminated with NTA derived from wastewaters, and through the use of consumer products containing NTA. A comparatively small number of people will be exposed to NTA during its manufacture and formulation. Based on the limited data available, it is expected the typical exposure via these routes will be low.

Drinking Water

The Canadian government established in late 1971 a national program to monitor NTA in surface and drinking waters following increases in NTA use corresponding to limitations on the phosphorus content of detergents. The drinking water monitoring data are contained principally in two reports: Matheson's (1977) report on the nationwide monitoring effort from 1972-1975 and Maliyandi, Williams and O'Grady's (1979) report on monitoring of 70 municipalities across Canada during the winter of 1976-77. Both reports indicate that continuous low level exposure (low ppb range) from Canadian drinking water exists.

Maliyandi et al. using an analytical method sensitive to 0.2 ug/l, found that the national mean value for NTA in drinking water was 2.82 ug/l, ranging from less than 0.2 ug/l to 24.5 ug/l (+1.53). Their sampling was conducted during the winter months, a time when the highest levels of NTA might be expected due to reduced biodegradation at temperatures of 10°C and below (Shannon et al., 1974). A grab sample was taken prior to treatment, just after treatment, and .5 and 1 mile beyond the treatment plant. The municipalities were chosen to be representative of the range of raw water quality, amount of drinking water consumed (i.e., population size), treatment process and geographic distribution. No effort was made in this work to select and study the NTA concentration in different types of water supplies. With maximum intake of 24.5 ug/l NTA and consumption of 2 liters of water per day, a person could ingest 49 ug NTA per day and less than 1.4 g over a 75-year lifespan.

Matheson (1977) summarized sampling runs conducted on municipal drinking water supplies throughout Canada by the Canadian Centre for Inland Waters (CCIW) and in Ontario by the Proctor and Gamble Company of Canada (P&G). The CCIW samples were four annual grab samples analyzed from the largest cities in each province with a method sensitive to 10 ppb. The P&G data are samples from the tap water and untreated river water above and below sewer outfalls at 13 Ontario cities; the samples were taken monthly from November

1971 to March 1975 and analyzed with a method sensitive to 1 ppb. CCIW results indicate relatively few samples in the detectable range (>10 ppb) and none of the samples contained more than 60 ppb NTA. Proctor and Gamble's study of 13 cities in southern Ontario (Monsanto and Proctor and Gamble, 1976) taking their water from rivers (6), wells (6) and Lake Ontario (1) showed a mean value of about 5 ug/l, with 96% of all samples less than 25 ug/l.

Maliyandi et al. compared their data (1976-77) with previous monitoring results (1972-1975) for 10 cities (Matheson, 1977). The comparison indicated that the most recent NTA concentrations are less than or equal to earlier values, suggesting that NTA does not appear to be accumulating in Canadian drinking water supplies, despite the increase in the industrywide average NTA content in detergents from 6% in 1972 to 15% in 1975-1977.

Several problems exist with the monitoring data available. With the exception of Proctor and Gamble's monitoring in Ontario, the available data come from spot checks taken at infrequent (annual) intervals of highly variable systems. Because of the high month-to-month variation seen in the 13 Proctor and Gamble cities, more frequent sampling at the other stations may be needed to assess the true exposure through drinking water. Furthermore, Matheson suggests that confidence limits of -50% to +100% are not unreasonable for the data he presents due to variations in analysis in different laboratories.

While the effect of the type of drinking water source is not clear, it is obvious that certain towns in Canada (e.g., Brantford, ON; Drummondville, QU; Lachine, QU; and Pierrefonds, QU) have consistently higher NTA concentrations in drinking water than other towns. Is this due to the type of drinking water source or perhaps the dilution rate or treatment efficiency of upstream sewage sources? Some effort was made in the Proctor and Gamble study to separate drinking water derived from rivers, ground water, and a large lake (Lake Ontario). Their data from southern Ontario show that drinking water from rivers influenced by sewage from upstream communities contained the highest median and maximum NTA levels. Matheson also noticed a higher frequency of detectable (>10 ppb) levels of NTA in drinking water from small rivers in Ontario. It appears that while most drinking water sources in Canada are relatively uncontaminated (<1 ppb) with NTA (Maliyandi et al., 1979), some populations are exposed to much higher levels (20-60 ppb). Any NTA monitoring effort in the U.S. should include a representative sampling from the different types of sources for drinking water.

One population at greater risk was identified by Matheson, namely those people obtaining drinking water from private shallow wells. Municipal ground water sources

showed no appreciable NTA contamination, probably because they are derived from deep aquifers some distance away from sewage sources. NTA readily degrades in aerobic soils, but it is the private wells close to saturated septic tank drainage fields that have been found to contain fairly high levels of NTA (up to 3.9 ppm) (Matheson, 1977). Elevated NTA levels would in these cases be connected with coliform contamination as well.

Levels of NTA in U.S. drinking water are not expected to be very different from the Canadian experience. Per capita detergent use is higher and per capita sewage flow is lower in the U.S., tending to make projected NTA concentrations in treatment plant effluent about twice as high in the U.S. (Winters, 1978). Removal efficiencies and dilution factors are expected to be the same as in Canada, but certain circumstances (e.g., warm waters with high organic loading) may be a special problem in the U.S. NTA levels in the low ug/l range are expected in U.S. drinking waters, but special attention should be paid to those cities on major rivers whose drinking water contains sewage effluent from upstream municipalities.

Consumer Exposure

The total direct exposure to NTA through use of consumer detergent products would include exposure from inhalation of detergent dust in the home; percutaneous absorption from contact with detergent, wash water, and residues on clothing; and ingestion of residues left on dishes and utensils.

Table 3 gives the estimated number of persons exposed and exposure amounts through each of these routes if NTA is used in all laundry and automatic and hand dishwashing detergents. Exposure by way of inhalation of detergent dust was based on median (average and 95 percentile (or maximum estimated), measured detergent dust levels, average lung capacity of men, women, and children and possible NTA detergent content (25%). Percutaneous absorption estimates use the 24 hour absorption rate for shaved rats, estimated exposure area of hand and forearm to washwater and median and 95 percentile exposure time. Absorption through NTA residues on clothing were determined using the measured concentration of NTA on laundered fabric, average skin area exposed (man, woman, child), and highest measured absorption efficiency for animal skin. Ingestion of NTA residues on dishes was based on measured desposition on dinnerware, estimated daily dinnerware use and percent of dinnerware area in contact with food. More detailed information on how the exposure rates were calculated can be found in a report by Midwest Research Institute (1979).

Table 3. Estimated Human Exposure to WTA Through Consumer Use of Detergent Products

Exposure Route	Number of Persons Exposed ¹	Exposure (ug WTA/day)	Remarks
Inhalation of detergent dust	176-76 million (laundry)	.07 - .38 ^{2,4}	
		.6 ug maximum short term exposure	
Absorption through contact with washwater	33 million (dishwashing)	.01 - .12 ^{2,4}	
	176-76 million (laundry)	8.75 - 17.5 ²	0.36 g/l WTA in laundry water
	176-76 million (dishwashing)	8.75 - 17.50 ²	0.50-0.75 g/l WTA in dishwater
Absorption through contact with detergent	176-76 million (laundry)	unknown	
	176-76 million (dishwashing)	unknown	
Absorption through contact with residues on clothing	215 million	.44 - 1.28 ³	
Ingestion of residues left on dishes	2 million (hand dishwashing without rinse)	947.5	
	213 million (hand dishwashing with rinse and towel dry)	4.9	0.01 ug/ew ² WTA on fabric
	Total, Consumer Use	22.9 - 41.7	maximum = 1004.3 ug/day (1% of the population)

¹ Assumes that only WTA products are in use.² Range based on midrange and high detergent use.³ Range based on skin area differences of adults and children.⁴ Range based on inhalation differences of average men, women and children.

Source: Midwest Research Institute, 1979.

Worker Exposure

Worker exposure can be conveniently divided into two areas: exposure during the actual manufacture and shipping of NTA, and exposure during the formulation of the detergent, i.e., combination of NTA with the surfactant and other detergent ingredients.

Current production methods at Monsanto and W. R. Grace (the only manufacturers at this time) utilize the highly toxic HCN (from acrylonitrile manufacture); consequently, most of the manufacture takes place in a closed system operated by remote control. Worker exposure is minimal, except during the drying, product packaging and bulk loading operations where dust levels are high (Midwest Research Institute, 1979). Manufacturers report that their hygiene standards require that the workers wear respirators during these operations (Hill et al., 1978; Kaelble et al., 1977).

Monsanto has reported (Kaelble et al., 1977) that NTA levels in air during bulk loading are between 0.13 and 1.12 mg/m³. The average worker spends 43-60 minutes per 8-hour day, at this operation. Another report (Hill et al., 1977) indicated that "normal line" workers are exposed to 0.1 to 0.5 mg NTA per workday, while bulk loaders may be exposed to an average of 3 mg NTA per workday if a respirator is not worn.

It is possible that workers could be exposed to other chemicals involved in NTA manufacture. Exposure to low levels of ammonia is possible for short periods of time; worker exposure on an 8-hour basis has been calculated to be less than 1.0 ppm on a time weighted average. As noted above, HCN exposure is not tolerated; this part of the process is handled under completely contained systems. Formaldehyde exposure is possible during bulk loading operations, but monitoring has shown worker exposure to be less than the 2 ppm ceiling (Midwest Research Institute, 1979).

The number of workers currently employed in NTA manufacture in the U.S. is 32. To manufacture 1 billion pounds, 93-120 workers would be required, assuming current technologies were used (Midwest Research Institute, 1979). Greater demand for NTA could result in a larger number of plants or companies manufacturing NTA, and a different manufacturing process having more or less exposure potential. Other patents for NTA manufacture exist (Midwest Research Institute, 1979), but the Grace patent (also used by Monsanto) is currently the only one in use.

Detergent formulation is the second area for exposure to NTA in the workplace. About 2500 workers are currently exposed to detergent dust during formulation and this number would not change with the introduction of NTA (MRI, 1979). According to Proctor and Gamble sources (Winters, 1978), the total dust level on a time weighted average is 1.38 mg/m³. The maximum NTA level would be .35 mg/m³, assuming all of the dust is detergent dust and NTA is 25% of the detergent formulation. Based on this value, extreme exposure would amount to 48.3 ug Na₂NTA/kg/day for an adult male (70 kg) and 35.7 ug Na₂NTA/kg/day for an adult female (54 kg). Industry sources believe typical exposure to be less than 10% of these figures.

Comparison of Exposure from Different Sources

The daily exposure to NTA from drinking water and consumer products is about the same, 5.6 ug/day (mean) and 13.82 - 24.15 (normal-worst case) respectively. Worker exposure to NTA during formulation and manufacture could be much higher, several hundred ug/day for normal line workers and several thousand ug/day for loaders not protected by respirators. However, because NTA and detergent production is largely automated, low numbers of workers (less than 3000) are expected to be exposed even during large scale NTA production (1 billion pounds annually). Exposure to NTA by way of drinking water and consumer products is expected to be low but widespread, affecting virtually the entire population. Table 4 presents this comparison.

Table 4. Summary of Potential NTA Exposure if Used in Detergent Products

Exposure Route	Number of Persons Exposed	Exposure (ug NTA/day)	Remarks
Drinking water	215 million	40.2 - 49 ^{b,g}	mean = 5.6 ug/day ^{b,g}
Consumer detergent products	215 million	22.9 - 41.7 ^e	
Workplace			
manufacture	98-120 ^{a,f}	<100 - 500 ^{c,f} 8,200 ^{d,f}	
formulation	1750 ^{a,f}	<338 - 3381 ^f	

^a Assumes 1 billion pounds of NTA manufactured annually.

^b Based on NTA levels found in Canadian drinking water and expected in U.S. at annual production levels up to 1 billion pounds.

^c Normal line workers without respirator.

^d Bulk loaders without respirator. Respirators, which are usually worn during this job, limit exposure to near zero.

^e See Table 3.

^f From MRI, 1979.

^g From Maliyandi et al., 1979.

Chapter V - Human Health Assessment of NTA

I. Metabolism of NTAA. Absorption, Excretion and Biotransformation1. Absorption

The metabolism and blood pressure effects of Na_2NTA in beagle dogs were studied by Bundy (1972). Approximately 89 percent of the oral dose, and 97 percent of the intravenous dose of labeled NTA was recovered after 72 hours. Of the orally administered dose, 80 percent was recovered in the urine and 3 percent in the feces, indicating that NTA is readily absorbed. Of the intravenous dose, 96% was recovered in the urine and a negligible amount in the feces, suggesting that enterohepatic circulation probably did not occur. Chromatography failed to reveal any metabolites of NTA in the urine, leading to the conclusion that biotransformation of NTA does not occur in the dog.

Bundy and Arnold (1973) studied the disposition of orally administered ^{14}C -NTA in eight human volunteers. Total recoveries of radioactivity after 120 hours averaged 89 percent of the administered dose, 77 percent from feces, approximately 12 percent from urine, and less than 0.1 percent from expired CO_2 . The blood concentration of NTA peaked 1-2 hours after dosing and was undetectable after 12 hours. While NTA was poorly absorbed, that which was absorbed was rapidly excreted in urine within 24 hours after NTA administration. Chromatography provided no evidence that NTA was metabolized, leading the authors to conclude that biotransformation had not occurred. The authors also suggested that it was reasonable to assume that there was no enterohepatic circulation of NTA in humans.

2. Distribution and Excretion

Chu and his coworkers (1978) studied the metabolic fate of NTA in the mouse. In one study, 5 male albino mice were given a single oral dose of ^{14}C -NTA (180 mg/kg). Serial samples of blood were taken for up to 8 hours after dosing, when the animals were sacrificed to obtain radioactivity counts in selected organs and tissues. In other studies, there were two groups of twenty mice, one receiving ^{14}C -NTA orally (180 mg/kg orally) and the other receiving ^{14}C -NTA intravenously (45 mg/kg). 1, 8 and 24 hours after ^{14}C -NTA administration, five animals from each group were exsanguinated and tissues were removed for determination of radioactivity.

Excretion studies were conducted by administering an oral dose to 5 mice. The animals were maintained in metabolic cages where urine and fecal samples were collected for 7 days. Food and water were available ad libitum. Experiments were also conducted in which bile duct-cannulated mice were administered intravenously ^{14}C -NTA, 4.5 mg/kg and 45 mg/kg intravenously. Bile samples were then obtained hourly for an 8 hour period and analyzed for radioactivity. Both orally and intravenously dosed animals showed the highest tissue distribution of NTA in the kidney, bladder and bone. Excretion studies with orally dosed mice revealed that approximately 99% of the dose was eliminated in 24 hours, with greatest excretion (approximately 95%) in the urine. Feces contained 3.5%, and 1% was found in the bile.

Tjalva (1972) also studied the distribution of radioactive label in mice given $\text{Na}_2\text{NTA-1-}^{14}\text{C}$ orally. Both sexes and some pregnant females were used. Treated mice were sacrificed serially and distribution of the labelled NTA was evaluated by autoradiography. The results showed that traces of radioactive label were found predominantly in the skeleton of fetuses. Label also appeared in the kidneys and bladder and, to a lesser extent, in the nasal mucosa, liver, blood and spleen. After intravenous dosing the intestinal contents also showed the label.

Michael and Wakim (1971) studied metabolic fate in fasted Sprague-Dawley, male rats by administering $\text{Na}_2\text{NTA-1-}^{14}\text{C}$ by gavage at pH 7.2. The rats spent the next 51 hours in metabolism cages with water and food ad libitum, and the ^{14}C in urine, feces, and expired air was determined. 95 percent of radioactivity was recovered--70% was from urine, 22% from feces, less than 1% from air, and 3% from the carcasses. After cannulation of thoracic and bile ducts, 4% was recovered from lymph and only 0.12% from bile, respectively. The biologic half-life of labelled NTA in blood and soft tissues was about 3 hours. After 48 hours, almost all label remaining was in bone, where concentrations varied from 40 to 8 mg of presumed NTA per gram of bone (tibia). The authors concluded that rats absorbed Na_2NTA readily and excreted most of it unchanged in the urine. What was not absorbed was excreted in the feces, under these conditions.

The authors also reported on the absorption and elimination of ^{14}C labeled NTA by the rabbit, dog and monkey. The dog absorbed the compound more rapidly and completely than the rat, judged by blood levels monitored one hour after dose and then daily for three days, whereas absorption was relatively poor by the rabbit and monkey. The data, however, is merely indicative of a trend, as only one animal/species was tested.

Tissue distribution studies indicate that the highest concentration of NTA occurs in the kidney, bladder and bone of exposed animals, but NTA rapidly disappears from the tissues on discontinuance of exposure. The rate of tissue elimination correlates well with blood clearance until the bone level reaches approximately 5 mg/g and the soft tissue levels approximate 0.5 mg/g when the NTA level remains relatively constant. This suggests tight binding to calcium in both bone and soft tissue, but the chronic toxicity studies show no deleterious effects from this low-level of residual NTA.

3. Biochemical Changes and Risk

No alterations in enzyme levels and activity have been found on dietary dosage with NTA for up to 90 days and 20,000 ppm in kidney, liver and blood systems (Thayer and Kensler (1973) and Michael and Wakim (1973)). Other metabolic alterations, such as the metabolism of sulfoproteins, or removing of chondroitin sulfate from the renal tubule epithelium did not suggest that any hazardous effects would be found after acute or low level exposure. However, these potential metabolic alterations on long term exposure to NTA may produce chronic toxicological effects, as indicated by urinary tract neoplasms occurring on diets containing 14,000 ppm of NTA.

In summary, these studies indicate that oral doses of the compound are excreted rapidly, predominantly through the feces and urine. The data indicate that absorption of the compound is species dependent. In this regard, studies with human volunteers indicate that man absorbs only 20-25% of the amount absorbed orally by most other species. Absorbed NTA has been found to be rapidly excreted, unchanged, in the urine. Biotransformation of the compound in species other than dogs and man has not been assessed. Oral absorption of NTA is relatively poor in man, biotransformation is not measurable, excretion is rapid, toxicity is low and exposure is also low. NTA, or its metabolites, are thus not a high risk at expected exposures for acute or subchronic effects.

II. Acute Effects of NTA

A. Oral Toxicity

According to the Senate Committee in 1970 (Epstein, 1970), there was no evidence that NTA detergents represented any significantly different acute hazard from that of phosphate detergents. The same may be said today, judging from more recent studies. In studies using dogs and monkeys (Nixon, 1971) levels of up to 5 g/kg of Na_2NTA produced rapid emesis and no deaths.

In the rat, which does not regurgitate, the oral LD_{50} is reported as 1470 mg/kg. (NIOSH, 1977). This falls in a classification of low acute toxicity, and confirms the judgement above that the acute hazard and risk of NTA to humans is very low.

B. Inhalation Toxicity

William Hopping of Proctor and Gamble, in a letter of June 25, 1979, reported several acute and four week repeated exposure studies performed in rats, guinea pigs and monkeys. Comparative inhalation toxicity studies were performed for different dose levels of NTA, sodium tripolyphosphate (STP) and their mixture (1:1). In these studies, pulmonary functions and biochemical, hematological and necropsy examinations were evaluated. No histopathological findings were reported. NTA was found to be less irritating to the respiratory tract and less toxic than STP. The letter from Proctor and Gamble is attached (Appendix B).

C. Eye/Dermal Irritation and Dermal Sensitization

NTA and its salts have been tested in several studies for subchronic cutaneous irritation. When applied to either abraded or intact skin of rabbits, an aqueous solution of 2.5% Na_3NTA (50 mg/kg/day) showed no adverse effects, whether administered for 20 or 65 treatments. Eleven percent of the sodium salt of NTA (Na_3NTA) in a detergent solution was similarly non-irritating to rabbit skin.

In primary irritation and sensitization studies in rabbits, a 1% solution of granular detergent with 1% Na_3NTA proved to be a mild irritant; the same formulation, however, without Na_3NTA produced equivalent results.

In human studies (patch test), primary irritation at a 10% to 1% level was extremely mild and there was no evidence of sensitization when challenge patches were applied. Other studies using a 5% solution showed no irritation even when applied to human subjects with skin lesions common in advanced scleroderma (Nixon, 1971; Rubin as cited by Mottola, 1974).

Nixon found that Na_3NTA , in varying concentrations in detergent solutions, produced conjunctivitis in rabbits when the eye was left unrinsed. However, this damage was attributable to the detergent rather than to NTA. (Nixon, 1971)

D. Acute Risks

The very high oral dosage needed to cause any toxic effect shows that the acute hazard from NTA exposure is low. Since man absorbs substantially less than other species, and is likely to regurgitate overdoses and rapidly excrete the absorbed portion unchanged, the risk to man from acute exposure is minimal.

III. Subchronic and Chronic Effects of NTA

A. Subchronic and Chronic Toxicity

The toxicity on continued exposure to NTA at various levels and routes of administration has been reviewed by official agencies several times (Woods Committee, 1972; IJC Task Force, 1977). It was generally concluded that ingestion of 0.5% or less in the diet for periods up to 2 years did not increase tumor incidence in rats, but other chronic toxic effects, such as nephritis and nephrosis could be observed (see e.g., Nixon et al. 1972). Biochemical and hematological parameters were not changed or returned to normal on continued treatment except at high levels of 0.15% or more in the diet. (Hopping, 1979, Appendix B) In such cases, the urinary zinc level was increased, dose dependent increases of urinary calcium excretion occurred, as well as crystalluria (CaNaNTA) and reversible vacuolation of the renal tubular epithelium (Nixon et al. 1972; Anderson, 1979). No significant toxic effects occurred below 0.15%.

B. Biochemical Effects

Thayer and Kensler (1973) presented data which described the effects of dietary NTA in rats on succinic dehydrogenase, cytochrome oxidase, alkaline phosphatase, acid phosphatase, diphosphopyridine nucleotide diaphorase, triphosphopyridine nucleotide diaphorase, and carbonic anhydrase. Analysis at up to 90 days of dietary exposure failed to show any consistent differences between control and NTA treated rats, except where a high level of NTA (20,000 ppm) had induced tissue or cellular damage.

Similarly, no effects on liver microsomal enzyme activity were noted in rats fed 20,000 ppm Na_2NTA in the diet for 20 days (Michael and Wakim, 1973).

C. Effects of NTA on Bone

Long term human exposure to NTA or its salts has been considered potentially harmful to the skeleton of the exposed population. This potential health hazard is attributable to the chemical properties of NTA as a potent chelating agent capable of binding calcium and presumably dissolving bone. The following studies were performed to address these issues. Thayer and Kensler (1973) presented unpublished data of the Proctor and Gamble Company showing that femur strength of dogs exposed to 5,000 ppm NTA in the diet for two years were not significantly different from controls. In addition, histological examinations failed to show any pathological effects produced by NTA at this exposure. Studies in mice (Greenblatt and Lijinsky, 1974) and the beagle dog (Bundy et al., 1973) also failed to demonstrate any structural differences in the bone of treated and control animals.

D. Influence of NTA on Heavy Metal Toxicity

Numerous investigations (Scharpf et al., 1972; Jacobson, 1972; Mahaffey and Goyer, 1972; Tandon et al., 1975; Michael and Wakim, 1973; Bundy et al., 1973; Garber and Wei, 1974; McClain and Slekiewka, 1975; Chu et al., 1977) have evaluated the effect of NTA on heavy metal toxicity i.e., cadmium, lead, manganese and mercury toxicity have been evaluated in combination with NTA. These authors concluded that based on clinical signs, organ weight ratios or pathological changes, there were no significant differences in toxicity between metals alone or in combination with NTA. When comparing body weight changes, however, the metals alone were more toxic than the metal plus NTA.

E. Chronic and Subchronic Risks of NTA

Absorption of NTA from oral ingestion, inhalation or dermal exposure is relatively poor in man, presumably due to its ionic character. In addition, low doses show no classical toxic effects in animals; the risk to man for such effects is therefore negligible at expected consumer, workplace and environmental levels (See Chapter IV).

IV. Mutagenic Effects of NTA

A. In Vitro and In Vivo Mutagenicity

Three studies (I.J.C. Task Force Report, 1977; Kramers, 1976; cited by Epstein, 1972) on the effects of NTA in Drosophila Melanogaster have been reported. Two reports

presented negative findings and the third showed weak mutagenic effects induced by "high concentrations."

The I.J.C. Task Force Report (1977) refers to unpublished reports on in vitro mutagen assays of NTA. All of these studies were described as generating "negative findings." Stine and Hardigree (1971 and 1972) and Stine and Adams (1974) have reported a series of studies of the mutagenic effects of NTA. None showed any evidence of mutagenic activity of NTA at concentrations up to 60,000 ppm.

Several dominant lethal studies in mice have been reported, but only two (Jorgenson *et al*, 1975 and Kihlman and Sturelid, 1970) have been adequately reported in the literature. The remainder have been briefly mentioned in secondary sources. No consistent responses occurred to suggest that NTA was mutagenic to the mouse by the dominant lethal test.

In summary, only one study shows weak mutagenic effects, based on the incidence of non-disjunction of sex chromosomes in *Drosophila melanogaster* larvae, at NTA concentrations ranging up to 40,000 ppm.

Recently, Spanggard and Tyson (1979) performed a mutagenic study with the NTA degradation product formed in high yield by treatment with chlorine (hypochlorite) solutions. The product N-formyliminodiacetic acid, did not cause any mutagenic response when tested in amounts ranging from 10 to 5000 mg per plate in the Ames assay using five strains of *Salmonella Typhimurium*, with and without metabolic activation.

The authors in these studies were seeking information to address the environmental and toxicological implications of NTA derivatives which were raised by the Woods Committee in 1972. As noted, the results of the mutagenic study conducted on the reaction product were negative. In addition, the subcommittee Report on NTA (NTP, 1980) has reviewed the Proctor & Gamble submission on mutagenicity and finds no problems with NTA.

B. Risk of Mutagenesis

The general negative responses in mutagenesis tests for NTA and the low expected exposure level indicate that NTA is unlikely to be an environmental mutagen.

V. Reproductive/Teratogenic Effects of NTA

A. Effects of NTA Alone

A major concern which led to the voluntary removal of NTA-containing detergents in the United States in 1970 came from a report indicating that NTA might enhance the embryotoxicity and teratogenicity of heavy metals, specifically cadmium and mercury (Chernoff and Courtney, 1970). Since that time, numerous studies have been conducted in mice, rats and rabbits to evaluate this potential (Tjalva, 1972; Nolen *et al.*, 1971 and 1972).

Tjalva (1972) exposed ten pregnant NMR mice to 0.2% NTA in the drinking water from days 6 to 18 of pregnancy. The data failed to show any abnormalities in offspring of treated female mice. A reduction in the mean fetal weight of the exposed group was noted, but that difference was not statistically significant.

Nolen *et al.* (1971) investigated the reproductive and teratogenic effects of Na₂NTA at 0.1 and 0.5% of the diet either continuously (to males and females) or during organogenesis (to females at days 6-15 of pregnancy). Two generations of rats were exposed under these conditions. Studies with New Zealand rabbits were conducted by administering 2.5, 25, 100, or 250 mg Na₂NTA/kg body weight daily via intubation on days 7 through 16 of gestation for one pregnancy. Parameters assessed included percentage of conceptions, number of stillborns, number of corpora lutea, resorptions, live fetuses, and skeletal and soft tissue defects. The main effect of dietary Na₂NTA, was growth depression in adults and weanling rats fed the highest level continuously.

The authors, based on the results of these studies, concluded that Na₂NTA was neither embryotoxic nor teratogenic to the species tested.

B. Effects of NTA on Heavy Metal Teratogenicity

Nolen *et al.* (1972) studied cadmium and mercury exposures in drinking water ranging from 0 to 4 mg/kg. Na₂NTA was administered up to 20 mg/kg to female Charles River rats for each level of metal. In other studies, the author exposed pregnant female rats to 4 mg/kg of either Cd or Hg, alone or in combination with 20 mg/kg Na₂NTA or sodium citrate, each day from days 6 to 15 of gestation. Experiments were also conducted with iron salts to determine the effects of these salts and the chelator, trisodium citrate, on the teratogenicity of mercury, cadmium and Na₂NTA mixtures.

The data did not indicate any increase in cadmium or mercury teratogenicity induced by either Na_2NTA or $\text{Na}_2\text{Citrate}$. Teratogenic effects of methyl mercury were reduced in Na_2NTA and FeCl_3 treated dams, but the authors attributed this to the protective effect of Fe^{3+} alone. The authors did note that Na_2NTA appeared to produce some protective effect against cadmium toxicity as shown by a significant increase in weight gain of dams fed CdCl_2 and Na_2NTA in contrast to CdCl_2 alone.

Scharpf and co-workers (1974 and 1975) also investigated the teratogenicity of cadmium chloride and methyl mercury hydroxide in Charles River COBS female albino rats in the presence and absence of NTA in high doses (80 mg CdCl_2 in combination with up to 160 mg NaCl /kg/day or up to 250 mg NTA/kg/day). The other test was at dosage levels of 1.5, 6.0 and 8.0 mg/kg/day CH_3HgOH , in combination with up to 38.7 mg/kg/day Na_2SO_4 or 9.4 up to 50.3 mg NTA/kg/day. The test materials were administered by gavage from days 9 through 19 of gestation. Dams were sacrificed on the twentieth day of gestation and necropsied for determination of various reproductive and teratogenic effects.

The data showed complete maternal mortality in rats administered 8.0 mg/kg Hg. In combination with either (1.5-6.0 mg/kg) there was a significant decrease in maternal mortality in the presence of NTA. The results of these extensive, well-designed and investigated studies show that ingestion of NTA does not increase toxicity or teratogenicity of ingested methyl mercury hydroxide in rats.

C. Reproductive/Teratogenic Risks

Since it has been shown that NTA, even in the presence of heavy metals, does not cause teratogenic or reproductive effects, there is little or no risk to humans from expected worker, consumer and environmental exposures.

VI. Oncogenic Effects of NTA

A. Oncogenesis

Prior to the National Cancer Institute (NCI) report on nitrilotriacetic acid (NTA and trisodium nitrilotriacetic acid, monohydrate ($\text{Na}_2\text{NTA} \cdot \text{H}_2\text{O}$), several investigators studied the carcinogenic potential of these compounds in rats and mice; no statistically significant difference could be noted in the number of tumors produced in the treated animals in

comparison to controls. The discrepancy between these results and those of the NCI feeding bioassay is most likely due to the use of smaller doses of NTA and its salts, and differences in the routes of administration employed.

The NCI feeding bioassay of NTA and Na_2NTA were carried out at the Stanford Research Institute (SRI) using Fisher 344 rats and at Litton Bionetics, Inc. using both Fisher 344 and B6C3F1 mice. Treatment with these compounds resulted in lesions of the urinary tract in both species which were characterized by primary tumors of epithelial origin, by hydronephrosis and/or nephritis in high dose rats and by nephritis in both high and low dose mice.

In the SRI study 200, 2,000 and 20,000 ppm of $\text{Na}_2\text{NTA} \cdot \text{H}_2\text{O}$ were fed to male and female rats for 24 months and the results were as follows. At the highest dose (20,000ppm), there was a statistically significant incidence of kidney tumors in male rats (9/24 treated vs 0/24 control; $p=0.001$), in tumors of the bladder in female rats (5/24 treated vs. 0/22 control; $p=0.011$), and in tumors of the ureter in both male and female rats (6/24 treated vs. 0/24 controls; $p=0.011$). At 2000 ppm only one female rat had a urinary system tumor; none of the males or females receiving 200 ppm $\text{Na}_2\text{NTA} \cdot \text{H}_2\text{O}$ displayed urinary system tumors.

In the Litton study, 7,500 ppm and 15,000 ppm of NTA and $\text{Na}_2\text{NTA} \cdot \text{H}_2\text{O}$ were fed to male and female rats for 18 months after which time they were switched to normal laboratory chow for 6 months. Using this treatment regimen $\text{Na}_2\text{NTA} \cdot \text{H}_2\text{O}$ induced tumors of the urinary tract in numbers too low to be statistically significant. However, the administration of 15,000 ppm of NTA produced 12/48 bladder tumors in female rats as compared to 0/18 in the controls ($p=0.014$).

In another Litton study employing both sexes of B6C3F1 mice, the same feeding protocol as stated above was used and the doses administered were 7,500 and 15,000 ppm of NTA and 2,500 and 5,000 ppm of $\text{Na}_2\text{NTA} \cdot \text{H}_2\text{O}$. Tumors of the kidney occurred in male mice at 15,000 ppm of NTA (24/44 treated vs. 0/20 controls; $p=0.001$).

Thus, in summary, both NTA and $\text{Na}_2\text{NTA} \cdot \text{H}_2\text{O}$ were shown to be carcinogenic to the kidneys and urinary tracts of both mice and rats at the highest doses tested.

B. Quantitative Oncogenic Risks of NTA Exposure

1. Human Exposures

Estimates of potential human exposure to $\text{Na}_2\text{NTA} \cdot \text{H}_2\text{O}$ (hereafter abbreviated as NTA) were obtained from Table 3, "Summary of Potential NTA Exposure if Used in Detergent Products" in Chapter IV, "Human Exposure". Each

of these estimated human exposures to NTA in $\mu\text{g-NTA/day}$ (micrograms of NTA per day) were converted to mg-NTA/kg/day (milligrams of NTA absorbed each day for each kilogram of the body weight of an animal each day) equivalents. The assumption was made that the average body weight of humans is 70kg.

2. Laboratory Animal Exposures

A 1977 National Cancer Institute (NCI) bioassay for the carcinogenicity of NTA conducted at Stanford Research Institute (SRI) using groups of 24 Fisher 344 rats tested at dietary concentrations of NTA of 0, 200, 2000, and 20,000 parts per million (ppm) for a 24-month period was used as the basis for the low-dose extrapolations required to quantify the carcinogenic risks to humans associated with potential NTA exposures. Although a number of animal bioassays for the carcinogenicity of various forms of NTA have been conducted in recent years, the SRI-conducted NCI bioassay was chosen because the form tested in this bioassay, the trisodium salt of NTA ($\text{Na}_3\text{NTA}\cdot\text{H}_2\text{O}$), is also the form used as a replacement for phosphates in detergents. Also, among the bioassays employing this form of NTA, the SRI bioassay provided the greatest range of dosage levels from which to perform an extrapolation.

Each of three non-zero dietary concentrations in this bioassay was converted to mg/kg/day to correspond with the units in which the estimated human exposures were expressed. The conversion was achieved by multiplying the ppm dietary concentration times the ratio of the assumed weight of the food eaten daily to the animal's own weight. For Fisher 344 rats this factor was assumed to be equal to .05 (5 percent) on the average (Anderson, 1979).

3. Statistical Significance

Tables 5a and 5b, respectively, present the tumor incidence data and statistical significance levels from the NTA bioassay by sex and dietary concentration for all tumor types and for urinary system tumors alone. Tumors of the urinary system, i.e. urinary bladder, ureter, and kidney, were of special interest because of the rare occurrence of these types of tumors in the Fisher 344 strain. In the NTA bioassay there was a complete absence of spontaneous urinary system tumors in the control groups, in marked contrast to the incidences found in the experimental groups at the highest dietary concentration.

Table 9a

Incidence of All Tumor Types and Statistical Significance Levels by Sex and Dietary Concentration for Data from ENE-Created MCF Intensity with $10, 100, 1000$ Administered to Fisher 344 Mice for 24 Weeks

Sex	Number of Animals with Any Tumor	Number of Animals Without Tumors	Total Number of Animals Receiving Dietary Concentration	Results from Statistical One-Tailed Fisher Exact Test (p-value)	Statistical Significance Two One-Tailed Dunnett t-statistic
Males					
Dietary Concentration					
0 ppm (0 mg/kg/day)	8	16	24		
200 ppm (10 mg/kg/day)	15	8	23	.0286	2.29 (p < .05)
2,000 ppm (100 mg/kg/day)	9	15	24	.5000	0.30 (p > .05)
20,000 ppm (1000 mg/kg/day)	18	6	24	.0042	3.03 (p < .005)
Females					
Dietary Concentration					
0 ppm (0 mg/kg/day)	13	11	24		
200 ppm (10 mg/kg/day)	17	7	24	.1857	1.46 (p > .05)
2,000 ppm (100 mg/kg/day)	15	9	24	.3851	.62 (p > .05)
20,000 ppm (1000 mg/kg/day)	19	5	24	.0623	1.85 (p > .05)

*All tumor types include tumors of the urinary system, lung, endocrine system and hepatopoietic system.

Incidence of Urinary System Tumors and Statistical Significance Levels by Sex and Dietary Concentration for Data from SH-1-Operated HCl Biosay with $10 \mu\text{M} \text{H}_2\text{O}$ Administered to Fisher 344 Rats for 24 Months

Values	Number of Animals with any Urinary System Tumors	Number of Animals without Urinary System Tumors	Total Number of Animals Receiving Dietary Concentration	Results from Statistical One-Tailed Fisher Exact Test (p-value)	Local Significance Test One-Tailed Bonferroni t-statistic
Dietary Concentration					
0 ppm (0 mg/kg/day)	0	24	24	p = .50000	0.00 (p > .05)
200 ppm (10 mg/kg/day)	0	23	23	p = .50000	0.00 (p > .05)
2,000 ppm (100 mg/kg/day)	0	24	24	p < .00005	7.98* (p < .005)
20,000 ppm (1000 mg/kg/day)	14	10	24		
Panel					
Dietary Concentration					
0 ppm (0 mg/kg/day)	0	24	24	p = .50000	0.00 (p > .05)
200 ppm (10 mg/kg/day)	0	24	24	p = .50000	0.52 (p > .05)
2,000 ppm (100 mg/kg/day)	1	23	24	p < .00005	6.81 (p < .005)
20,000 ppm (1000 mg/kg/day)	13	11	24		

The one tailed Fisher Exact Test (Dixon, 1977) was used to determine whether the tumor incidence of an experimental group at a given dietary concentration was significantly greater than the tumor incidence in the respective control group. Tumor incidences for the experimental groups at each dietary concentration were simultaneously compared with the spontaneous tumor incidences in the appropriate control groups. The Bonferroni inequality (Miller, 1966) was applied to ensure an overall significance level of $\alpha = 0.05$ for each set of simultaneous comparisons. The Bonferroni inequality requires that for statistical significance to be achieved in a given comparison at the 5% level the p value from the Fisher Exact Test must be less than or equal to $.05/k$ where k is the number of nonzero dietary concentrations. For each of the comparisons made in Table 5a and 5b, $k = 3$ and $.05/k = .017$.

When tumors of all types (urinary system, lung, endocrine, hematopoietic) were included (Table 5a), only the tumor incidence for male rats exposed at a dietary concentration of 20,000 ppm NTA was significantly greater than the spontaneous incidence. When tumor type was restricted to urinary system tumors (Table 5b), tumor incidences for both male and female rats exposed at dietary concentrations of 20,000 ppm NTA were significantly greater than the spontaneous incidences.

When the tumor incidences of experimental groups at three or more dietary concentrations are simultaneously compared to the tumor incidence in an appropriate control group, the Bonferroni inequality as applied to the one-tailed Fisher Exact Test becomes increasingly conservative. As the number of non-zero dietary concentrations in a bioassay becomes large, the critical region for each separate one-tailed Fisher Exact Test is drastically reduced. The one-tailed Dunnett test (Dunnett 1955, 1964) maintains a given overall significance level, while allowing for large numbers of simultaneous comparisons without impacting on the critical region of each separate comparison.

These differences of statistical power in the one-tailed Dunnett test and the Bonferroni inequality became especially important in the determination of the statistical significance of the incidence of all tumor types in male rats exposed to a dietary concentration of 200 ppm NTA. The p-value for this comparison by the Fisher Exact Test is Table 5a was .0286. The adjustment with the Bonferroni inequality indicated that the incidence for all tumor types at the dietary concentration of 200 ppm NTA was not significantly different ($.0286 > .017$) from the spontaneous incidence. However, Dunnett's test indicated that the difference in

incidence for all tumor types in this instance was significant. The inconsistent nature of these results indicated that the incidence for all tumor types in male rats exposed at a dietary concentration of 200 ppm NTA may not be safely regarded as not significantly different from the spontaneous incidence.

4. Quantitative Risk Estimation

Two separate stages were involved in deriving quantitative estimates of carcinogenic risk to humans. The first stage involved the extrapolation of a dose-response curve for Fisher 344 rats over a region of extremely low dietary concentrations of NTA, far below the concentrations used in the NTA bioassay.

In the first stage, two separate low-dose extrapolation procedures were used to derive a dose-response curve. These extrapolations were performed separately with incidence data for male and female rats and for tumors of all types and urinary system tumors alone. One extrapolation procedure used was the "one-hit" dose-response model proposed by the EPA Carcinogen Assessment Group (CAG) (Anderson 1979). Following is a brief discussion of the theory underlying the one-hit model. In this discussion "tumor incidence" is synonymous with "risk" and "dietary concentration" is synonymous with "dosage". Assuming that some risk of cancer results from even a slight exposure to a carcinogen, the exponential probability law;

$$(1) P = 1 - e^{-\lambda d}$$

gives the probability, P , that a carcinogen at a dosage, d , will induce a tumor in these animals. It may be the case that some of the tumors in the treatment group were not induced by the carcinogen, but had developed spontaneously. Where P is the probability that a tumor develops spontaneously in a control group and P_c is the probability that a tumor develops in the treatment group, the probability that a tumor does not develop in the treatment group was shown by Abbott (1925) to be

$$(1 - P_t) = (1 - P_c) (1 - P)$$

Solving,

$$(2) P = \frac{P_t - P_c}{1 - P_c}$$

Substituting (2) into (1), gives the probability of observing a tumor in the treatment group,

$$(3) P_t = 1 - (1 - P_c)e^{-\lambda d}$$

Solving (3),

$$\lambda = \frac{1}{d} \ln (1 - P_c) / (1 - P_c).$$

At very low dosages, P is almost directly proportional to the dosage d and λ will be the slope of the dose-response curve obtained when P is plotted against values of d close to zero. Because this form of the one-hit model approximates a straight line through the origin at very low dosages, it is often referred to as the linear non-threshold dose-response model. It states that any exposure to a carcinogenic substance will result in some risk of tumor incidence, and the risk or probability of cancer induction at low dosages increases almost linearly with increasing dose.

Use of the CAG one-hit model with data from the NTA bioassay required that the treatment group be defined as the group at the lowest dietary concentration whose tumor incidence had been shown to be a statistically significant increase over the spontaneous tumor incidence in the control group. Separate extrapolations were performed with the CAG one-hit model using the incidence for all tumor types in male Fisher 344 rats at the 200 ppm and 20,000 ppm dietary concentrations of NTA due to the inconsistent answer provided by the one-tailed Fisher Exact Test and the one-tailed Dunnett test as to the statistical significance of the 200 ppm NTA concentration.

The second extrapolation procedure used to derive a dose-response curve was a computer-based one-hit model developed by Dr. Charles Brown of the Biometry Branch, Division of Cancer Cause and Prevention, National Cancer Institute. The mathematics of the Brown one-hit model differ from the CAG one-hit model in that Brown's model : takes into account the tumor incidences at all dietary concentrations simultaneously without regard to the statistical significance of any. It is especially useful with the NTA bioassay as it does not demand an answer to the question of the statistical significance of the incidence for all tumor types in male Fisher 344 rats exposed at the 200 ppm dietary concentration of NTA. The computer program for the Brown one-hit model also allowed derivation of values of λ by the CAG one-hit model. Therefore, 95% and 99% upper confidence limits were placed on all derived values of λ regardless of the form of the one-hit model used.

The larger of the value of λ the steeper is the dose-response curve at low-dosages-hence a greater assumed sensitivity of Fisher 344 rats to NTA exposure, in that a lower dietary concentration would be associated with a given tumor incidence; or conversely, a given dietary

concentration would be associated with a greater tumor incidence. By either the CAG one-hit model or the Brown one-hit model, the values of λ derived using male Fisher 344 rat data were consistently greater than the values of λ similarly derived using female Fisher 344 rat data. Therefore, to incorporate an additional measure of conservatism, the male Fisher 344 rat data alone were chosen for all calculations involved in the derivation of final estimates of carcinogenic risk to humans associated with potential NTA exposures.

The second stage in the derivation of estimates of carcinogenic risks associated with potential human exposure to NTA, involved the transformation of each value of λ for Fisher 344 rats to a value of λ for humans. This transformation was accomplished with a species conversion factor. This species conversion factor is based upon the knowledge that the specific dose in mg/kg/day of a direct acting agent required to produce an effect in humans is smaller than the specific dose of that agent that would be required to produce a similar effect in a given animal species. If dietary concentrations or exposure levels are expressed in mg/kg/day, then the potency of a chemical or direct-acting drug in humans is higher than in an animal by the ratio:

$$\left[\frac{\text{Average human weight}}{\text{Average animal weight}} \right]^{1/3}$$
 If the average human weight is assumed to be 70kg (70,000g) and the average weight of a Fisher 344 rat is assumed to be 350g then the conversion factor is $(70,000g/350g)^{1/3} = (200)^{1/3} = 5.85$ (Anderson, 1979).

Each point estimate of the value λ from the Fisher 344 male rat data, along with associated 95% and 99% upper confidence limits on λ was multiplied by the species conversion factor of 5.85 to yield a point estimate of the value of λ for humans along with associated 95% and 99% upper confidence limits. To arrive at final quantitative estimates of carcinogenic risk from potential human exposures to NTA, each point estimate of λ and associated upper 95% confidence limits was combined with the range of exposure estimates, d , and applied to (1)

$$P = 1 - e^{-\lambda d}$$

the exponential probability law. The respective resultant values of P are the point estimates and upper 95% and 99% confidence limits of risk or probability that a lifetime of human exposure to NTA at dosage level, d , would induce a tumor in a human so exposed.

Tables 6a, 6b, and 6c present point estimates and upper 95% and 99% confidence limits of carcinogenic risk for all tumor types associated with a range of potential exposures to NTA. The risks in Table 6a were derived by the Brown one-hit model. Tables 6b and 6c, present risk estimates derived by the form of the CAG one-hit model using the tumor incidences at the 200 ppm and 20,000 ppm dietary concentrations, respectively. All risk estimates or probabilities of tumor incidence are presented in scientific notation. For example, a risk of $2.13\text{E-}5$ (2.13×10^{-5}) for workplace-formulation exposure is roughly equivalent to a risk or incidence of 2 per 100,000 or 1 in 50,000.

Tables 7a and 7b present point estimates and upper 95% and 99% confidence limits of carcinogenic risk for urinary system tumors associated with a range of potential exposures to NTA. The risks in Table 7a were derived by the Brown one-hit model. Table 7b presents risk estimates derived by the CAG one-hit model using the tumor incidence at the 20,000 dietary concentration (the only concentration at which a statistically significant incidence of urinary system tumors occurred in males).

Tables 7b generally provides that highest estimates of risk from NTA exposure. The worst case exposure situation occurs with workers in the detergent formulation process, who are also exposed at home as consumers and through their drinking water. The risk for such individuals is 2.5×10^{-4} , i.e., one person in 4000 exposed over his lifetime in this manner would contract a tumor of the urinary tract. This risk seems quite high, however, the population of workers so exposed (population at risk) in the United States is only 2,500. Thus, in such a population less than one person (.625 individuals) could be expected to be affected if all 2,500 were exposed for a lifetime. The risks derived are admittedly a conservative attempt to place an upper bound on the oncogenic risk. The worker exposure could probably also be lowered substantially through mandatory requirements for the wearing of dust masks. Thus, even in the "worst-case" the expected number of individuals with cancers induced by NTA exposure is extremely small. The risks to the general population through drinking water are quite low, 3.58×10^{-6} , or roughly 1 in 500,000. Table 3b presents additional risks for various plausible combinations of exposure situations. The original exposure estimates and populations at risk are in Chapter 4, "Human Exposure." Bear in mind that the risks presented in Table 7b are upper bounds on the oncogenic risk and that the actual risks are likely to be much lower.

WAS OBTAINED FOR ALL THESE TESTS (1/)

Number of Animals		Type		Sex		Age		Weight		Height		Length		Chest		Tail		Ear		Foot		Claw		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney		Bladder		Stomach		Intestine		Pancreas		Gallbladder		Thyroid		Adrenal		Pituitary		Hypothalamus		Hypophysis		Pineal		Thalamus		Hypocampus		Caudate		Nucleus		Striatum		Globus		Cerebrum		Cerebellum		Medulla		Spinal		Nerve		Muscle		Bone		Cartilage		Skin		Fur		Bone		Teeth		Milk		Semen		Uterus		Ovary		Testis		Spleen		Liver		Kidney	
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11/ Interstitial-cell tumors of the testes were not included due to their high incidence in older age rates.

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"And the engine" to better-out leaders not wearing respiratory, provided a clothing to suitably worn.

WILLIAMSON COUNTY, MISSOURI

...on the basis of a comparison of the results of the two experiments. The results of the two experiments are compared in Table I. The results of the two experiments are compared in Table I.

Chemical Name	Type	Point Estimate	NO ₂ -NITRATES 1971-1972 1973-1974 1975-1976 1977-1978 1979-1980 1981-1982 1983-1984 1985-1986 1987-1988 1989-1990 1991-1992 1993-1994 1995-1996 1997-1998 1999-2000 2001-2002 2003-2004 2005-2006 2007-2008 2009-2010 2011-2012 2013-2014 2015-2016 2017-2018 2019-2020 2021-2022 2023-2024 2025-2026 2027-2028 2029-2030 2031-2032 2033-2034 2035-2036 2037-2038 2039-2040 2041-2042 2043-2044 2045-2046 2047-2048 2049-2050 2051-2052 2053-2054 2055-2056 2057-2058 2059-2060 2061-2062 2063-2064 2065-2066 2067-2068 2069-2070 2071-2072 2073-2074 2075-2076 2077-2078 2079-2080 2081-2082 2083-2084 2085-2086 2087-2088 2089-2090 2091-2092 2093-2094 2095-2096 2097-2098 2099-2100 2101-2102 2103-2104 2105-2106 2107-2108 2109-2110 2111-2112 2113-2114 2115-2116 2117-2118 2119-2120 2121-2122 2123-2124 2125-2126 2127-2128 2129-2130 2131-2132 2133-2134 2135-2136 2137-2138 2139-2140 2141-2142 2143-2144 2145-2146 2147-2148 2149-2150 2151-2152 2153-2154 2155-2156 2157-2158 2159-2160 2161-2162 2163-2164 2165-2166 2167-2168 2169-2170 2171-2172 2173-2174 2175-2176 2177-2178 2179-2180 2181-2182 2183-2184 2185-2186 2187-2188 2189-2190 2191-2192 2193-2194 2195-2196 2197-2198 2199-2200 2201-2202 2203-2204 2205-2206 2207-2208 2209-2210 2211-2212 2213-2214 2215-2216 2217-2218 2219-2220 2221-2222 2223-2224 2225-2226 2227-2228 2229-2230 2231-2232 2233-2234 2235-2236 2237-2238 2239-2240 2241-2242 2243-2244 2245-2246 2247-2248 2249-2250 2251-2252 2253-2254 2255-2256 2257-2258 2259-2260 2261-2262 2263-2264 2265-2266 2267-2268 2269-2270 2271-2272 2273-2274 2275-2276 2277-2278 2279-2280 2281-2282 2283-2284 2285-2286 2287-2288 2289-2290 2291-2292 2293-2294 2295-2296 2297-2298 2299-2300 2301-2302 2303-2304 2305-2306 2307-2308 2309-2310 2311-2312 2313-2314 2315-2316 2317-2318 2319-2320 2321-2322 2323-2324 2325-2326 2327-2328 2329-2330 2331-2332 2333-2334 2335-2336 2337-2338 2339-2340 2341-2342 2343-2344 2345-2346 2347-2348 2349-2350 2351-2352 2353-2354 2355-2356 2357-2358 2359-2360 2361-2362 2363-2364 2365-2366 2367-2368 2369-2370 2371-2372 2373-2374 2375-2376 2377-2378 2379-2380 2381-2382 2383-2384 2385-2386 2387-2388 2389-2390 2391-2392 2393-2394 2395-2396 2397-2398 2399-2400 2401-2402 2403-2404 2405-2406 2407-2408 2409-2410 2411-2412 2413-2414 2415-2416 2417-2418 2419-2420 2421-2422 2423-2424 2425-2426 2427-2428 2429-2430 2431-2432 2433-2434 2435-2436 2437-2438 2439-2440 2441-2442 2443-2444 2445-2446 2447-2448 2449-2450 2451-2452 2453-2454 2455-2456 2457-2458 2459-2460 2461-2462 2463-2464 2465-2466 2467-2468 2469-2470 2471-2472 2473-2474 2475-2476 2477-2478 2479-2480 2481-2482 2483-2484 2485-2486 2487-2488 2489-2490 2491-2492 2493-2494 2495-2496 2497-2498 2499-2500 2501-2502 2503-2504 2505-2506 2507-2508 2509-2510 2511-2512 2513-2514 2515-2516 2517-2518 2519-2520 2521-2522 2523-2524 2525-2526 2527-2528 2529-2530 2531-2532 2533-2534 2535-2536 2537-2538 2539-2540 2541-2542 2543-2544 2545-2546 2547-2548 2549-2550 2551-2552 2553-2554 2555-2556 2557-2558 2559-2560 2561-2562 2563-2564 2565-2566 2567-2568 2569-2570 2571-2572 2573-2574 2575-2576 2577-2578 2579-2580 2581-2582 2583-2584 2585-2586 2587-2588 2589-2590 2591-2592 2593-2594 2595-2596 2597-2598 2599-2600 2601-2602 2603-2604 2605-2606 2607-2608 2609-2610 2611-2612 2613-2614 2615-2616 2617-2618 2619-2620 2621-2622 2623-2624 2625-2626 2627-2628 2629-2630 2631-2632 2633-2634 2635-2636 2637-2638 2639-2640 2641-2642 2643-2644 2645-2646 2647-2648 2649-2650 2651-2652 2653-2654 2655-2656 2657-2658 2659-2660 2661-2662 2663-2664 2665-2666 2667-2668 2669-2670 2671-2672 2673-2674 2675-2676 2677-2678 2679-2680 2681-2682 2683-2684 2685-2686 2687-2688 2689-2690 2691-2692 2693-2694 2695-2696 2697-2698 2699-2700 2701-2702 2703-2704 2705-
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[illegible]

Intermittent-cell tumors were not included due to their high

The value required can be loosely described as the average square root of the values required by each replicator. Replicators are not regulated by GABA, however Monodant has indicated

[illegible]

that protection directed to country users.

ASSOCIATED WITH ESTIMATED BEHAVIOR TO NITRILATE/INACTIC ACID, THIOSODIUM SALT, MONOMERATE (H₂ST₂ST₂)

Exposure Estimate Type (Amount) (1/1)	NO. OF DAYS PER YEAR OF EXPOSURE (1/2)		ESTIMATED BEHAVIOR TO NITRILATE/INACTIC ACID, THIOSODIUM SALT, MONOMERATE (H ₂ ST ₂ ST ₂)		RISK ESTIMATE (1/3)
	Estimate	Estimate	Estimate	Estimate	
Drinking water alone (1.4E-3 mg/L/day) (1.4E-4 mg/L/day)	4.10E-3 3.38E-4		4.10E-3 3.38E-4	4.10E-3 3.38E-4	3.37E-3 6.63E-4
Consumer Exposure alone (1.31429E-4 mg/L/day) (1.31429E-4 mg/L/day)	1.62E-6 3.08E-6		1.62E-6 3.08E-6	1.62E-6 3.08E-6	2.92E-6 5.49E-6
Manufacture-manufacture alone (1.428571E-3 mg/L/day) (1.428571E-3 mg/L/day)	3.31E-6 3.46E-5		3.31E-6 3.46E-5	3.31E-6 3.46E-5	3.32E-6 6.56E-5
Manufacture-manufacture alone (1.31429E-4 mg/L/day) (1.31429E-4 mg/L/day)	6.00E-6 3.47E-5		6.00E-6 3.47E-5	6.00E-6 3.47E-5	1.00E-5 6.42E-5
Consumer plus drinking water (1.31429E-4 mg/L/day) (1.31429E-4 mg/L/day)	2.03E-6 6.43E-6		2.03E-6 6.43E-6	2.03E-6 6.43E-6	3.46E-6 1.19E-5
Manufacture-manufacture plus drinking water (1.31429E-4 mg/L/day) (1.31429E-4 mg/L/day)	7.72E-6 4.01E-5		7.72E-6 4.01E-5	7.72E-6 4.01E-5	1.39E-5 3.59E-5
Manufacture-manufacture plus drinking water (1.31429E-4 mg/L/day) (1.31429E-4 mg/L/day)	4.01E-5 6.01E-5		4.01E-5 6.01E-5	4.01E-5 6.01E-5	3.59E-5 5.49E-5
Manufacture-manufacture plus drinking water (1.31429E-4 mg/L/day) (1.31429E-4 mg/L/day)	2.51E-5 2.51E-5		2.51E-5 2.51E-5	2.51E-5 2.51E-5	4.52E-5 4.52E-5
Manufacture-manufacture plus drinking water (1.31429E-4 mg/L/day) (1.31429E-4 mg/L/day)	8.30E-6 4.32E-5		8.30E-6 4.32E-5	8.30E-6 4.32E-5	1.49E-5 3.59E-5
Manufacture-manufacture plus drinking water (1.31429E-4 mg/L/day) (1.31429E-4 mg/L/day)	6.04E-6 6.04E-6		6.04E-6 6.04E-6	6.04E-6 6.04E-6	1.00E-5 1.00E-5
Manufacture-manufacture plus drinking water (1.31429E-4 mg/L/day) (1.31429E-4 mg/L/day)	2.48E-5 3.51E-5		2.48E-5 3.51E-5	2.48E-5 3.51E-5	4.42E-5 6.42E-5

(1/2) The values reported are the "average exposure" and "median exposure", respectively.
 (1/3) The values reported are the "average exposure" and "median exposure", respectively.
 (1/4) The values reported are the "average exposure" and "median exposure", respectively.
 (1/5) The values reported are the "average exposure" and "median exposure", respectively.

(1/6) The values reported are the "average exposure" and "median exposure", respectively.

the chemical induced vacuoles. Also, the number of animals used to demonstrate the reversibility of this vacuolization process were too small, and an appropriate NTA control group was not used for the entire course of the experiment. Consequently, the P&G conclusions may not be justifiable. Also, to date, there is no proven relationship between a threshold for vacuolization and neoplasia. In addition, EPA recognizes that the data submitted by P&G are inadequate to make any conclusions concerning a threshold level for carcinogenesis by NTA.

2. The next issue involves the correlation between transitional cell carcinomas of the bladder and the NTA crystallurias. P&G states that the dose required to cause microcrystals of CaNTA correspond almost exactly to the dose of NTA required for the induction of neoplasms of the urinary tract resulting between crystalluria and carcinogenesis accompanied by the implication that a threshold dose for carcinogenesis exists. NTP has stated that there are no data available to establish crystalluria as an etiologic factor in carcinogenesis in those cases in which such a relationship has been suggested such as NTA, saccharin, and 4-ethyl-sulfonylnaphthalene-1-sulfonamide. Also, NTP refers to a study carried out by the National Institute of Environmental Health Sciences (NIEHS), in which renal tumors were found in rats given $\text{Na}_2\text{NTA} \cdot \text{H}_2\text{O}$ in drinking water at 10,000 ppm, a dose well below the amount considered by P&G to be the threshold level (NEISH, 1974). Unfortunately, time did not allow for a formal NRD review of the NIEHS study, but a cursory examination did reveal a questionable procedure in their protocol. Two groups of rats were used for this study--the body weight for the Group I rats was 70 grams and the Group II rats weighed 350 grams at the start of the experiment. It is conceivable that this large variation in weight and undoubtedly age of the animals at the onset of the study could affect the outcome of the experimental results. Nevertheless, NTP presents several arguments against attributing the carcinogenic effect of NTA to crystalluria and these include: the absence of grossly visible urinary calculi in animals with tumors, and the absence of urinary tract tumors in animals with other kinds of crystalluria (e.g. Dalmatian dogs excrete large quantities of uric acid crystals in the urine due to an inherited metabolic defect).

3. The P&G report also alleges that the chelating ability of NTA causes depletion of extracellular calcium and further "stripping" of calcium from renal cells. The results of such an occurrence are hematuria, hydronephrosis, diuresis and altered mineral excretion which lead to transitional cell carcinoma of the renal pelvis. The NTP committee has concluded that this mechanism has not been proven. Also, calcium homeostasis is under fine hormonal regulation, and it is likely that the body's storage pool would become depleted even in the presence of a chelating agent like NTA.

C. Proctor and Gamble Report and NTP Responses

In March, 1979, the Proctor and Gamble Company released a statement entitled "NTA and Carcinogenesis - The Dose Response Curve." (Proctor and Gamble, 1979). This report was an attempt to prove that the urinary tract tumors appearing in rats, following chronic treatment with large doses of NTA, are not the result of the primary carcinogenic action of this compound, but most probably a consequence of damage which occurs in the urinary tract when the animal is required to excrete high concentrations of NTA. Proctor and Gamble suggest that NTA is not a direct carcinogen. The urinary tract alterations which appear to result from extraction of divalent metal ions from the body by NTA, the formation of precipitates of NTA salts and the presence of uncomplexed NTA could induce such conditions as hydronephrosis, hematuria, crystalluria and disruption of mineral excretion which would be the causative factors in the production of urinary tract tumors.

Proctor and Gamble conducted a two year bioassay using Charles River rats fed 0.03% (300 ppm), 0.15% (1500 ppm) and 0.5% (5,000 ppm) $\text{Na}_2\text{NTA} \cdot \text{H}_2\text{O}$ and 0.5% (5,000 ppm) CaNaNTA in the diet. At 5000 ppm $\text{Na}_2\text{NTA} \cdot \text{H}_2\text{O}$, there was a small incidence of tubular cell neoplasia which was not statistically significant. At 300 ppm, the kidneys were indistinguishable from controls. However, at 1500 ppm, the kidneys displayed degenerative changes as early as six months; these changes did not progress to frank tumors within the two year time period.

The data generated by the Proctor and Gamble study and the NCI studies appears to indicate that statistically significant incidences in urinary tract tumors were found only at the highest doses employed by NCI. However, EPA realizes that this conclusion is not unequivocal, since the number of animals per test group is considered to be inadequate. Proctor and Gamble subsequently made statements regarding the proposed mechanism for the formation of these neoplasias. The kidney transitional cells tumors which appear predominantly in male rats receiving the highest dose level of $\text{Na}_2\text{NTA} \cdot \text{H}_2\text{O}$ are accompanied by hematuria, diuresis, hydronephrosis and exhaustion of the calcium excretion capacity. Proctor and Gamble postulates that the failure of male rats to mobilize enough calcium to accompany the NTA upon excretion leads to exhaustion of the calcium supply in the body along with sufficient amounts of uncomplexed NTA to cause degenerative and proliferative changes which ultimately lead to the formulation of transitional cell tumors. In addition, they correlate the appearance of tumors of the bladder, which occur predominantly in female rats, with crystalluria. Crystal formation in the urine is perhaps due to a greater propensity of females to supply calcium for urinary excretion, thereby forming crystals of CaNaNTA which precipitate in the bladder.

Although these may be reasonable explanations for what is seen to occur in NTA treated rats, there are no literature reports with experimental data to verify the hypothesis that it is these physiological alterations which are the primary causative factors for tumorigenesis and not a direct action of NTA.

However, Proctor and Gamble enhance their argument regarding the indirect carcinogenic effects of NTA by showing that extensive mutagenicity testing of this substance has failed to establish that NTA produces DNA alterations in cells. A variety of tests have given negative results and those few results which have been suggestive of mutagenic activity were reversed by the addition of mineral supplements. Thus, there are indications that the effects seen could most likely be attributed to the chelation of essential minerals by NTA.

Based on all the above information and the anticipated human exposure obtained from monitoring studies conducted in Canada, the Proctor and Gamble Company has concluded that the dose of NTA that an average person would consume daily via the drinking water would be 3×10^{-8} times less than the dose fed daily to rats for 2 years which produced no degenerative changes in the kidney (referred to as the no effect level dose). Therefore, they feel that the risk of inducing cancer in humans exposed to NTA is "vanishingly" small.

The National Toxicology Program (NTP) has published a subcommittee report entitled "Review of Proctor and Gamble Statement Regarding Carcinogenesis of NTA" which evaluates the hypotheses proposed by the Proctor and Gamble (P&G) Report concerning the mechanism of tumor induction by NTA. (NTP, 1980)

1. The first issue addressed concerns the appearance of renal tubular vacuoles and hyperplasia. Proctor and Gamble identifies such physiological alterations by light microscopy at the 1500 ppm dose of $\text{Na}_2\text{NTA} \cdot \text{H}_2\text{O}$ whereas the lower dose of 300 ppm shows no difference in urinary tract tissue relative to controls. Thus, a threshold dose for vacuologenesis is suggested. Also, P&G demonstrate that the intense vacuolization, produced by high doses of both the acid and salt form of NTA after 7 weeks of treatment, can be reversed upon termination of the chemical feeding.

In response, the NTP report states that a certain amount of vacuoles are normally present in renal tubular cells, and ultrastructural analysis, as opposed to light microscopy, would be a more definitive technique for identifying

4. In an oral presentation and unpublished report, P&G proposes that high amounts of ingested NTA cause excessive tubular resorption of ionic zinc resulting in tubular cell damage. NTP questions the validity of the assumption that changes in renal cell morphology lead to carcinogenesis, since no such relationship has yet been demonstrated. Also, P&G is, by their statement, suggesting a primary role of zinc in carcinogenesis; this relationship has not been demonstrated; and there is currently no evidence in the literature to indicate zinc as a causative factor in tumorigenesis.

The NTP report contains a final summary describing conceptual support for carcinogenesis resulting from adverse physiological alterations; it attempts to correlate these concepts to the mechanism for tumor production by NTA.

There are two proposed mechanisms for carcinogenesis: 1) genetic, 2) non-genetic. The first implies that a chemical interacts with cellular DNA causing mutagenic effects, which eventually lead to a tumor. It has been shown that NTA is not mutagenic at doses which would be of concern to an exposed population. Therefore, this genetic mechanism may not be the explanation for NTA carcinogenicity. Regarding the non-genetic mechanism, there is no evidence that NTA, or its trisodium salt, affect immunologic or endocrine functions in animals; the possibility that NTA may be a tumor promoter appears not to have been investigated. However, there is the possibility that NTA exerts its effects through physical rather than chemical properties, and this is based on the finding of crystalluria in dosed animals. There has been some research conducted in which foreign objects have been implanted in hollow organs, mostly bladder, and tumor formation was studied. Tumor production was related to size and surface structure of the foreign body; fragmented materials or microcrystalluria have not yet been shown to be carcinogenic under natural or experimental conditions in any animal species. This information, accompanied by other findings presented previously in the body of this paper, argue against attributing the carcinogenic effects of NTA to crystalluria. NTA may, however, exert a carcinogenic effect through its irritation of urinary epithelium leading to increased DNA synthesis and mitotic activity.

Finally, drinking water monitoring studies correlated with human absorption data of NTA allowed for the calculation that the physiological dose to man would be less than 0.07 mg/kg/day. Using a linear extrapolation based on this data and the data from studies which have shown an increase in urinary tract tumors in both sexes of mice and rats at high dosages, the maximum potential urinary tract tumor risk in rodents is estimated to be less than 2 in ten million. From this number, it appears that the risk is minimal. However, if NTA is used and released to the environment in large quantities, new monitoring studies would have to be conducted to determine if such large scale use/release would increase the amount of NTA in drinking waters and elevate the risk of carcinogenesis in man.

VI. Environmental Effects Assessment

It can be stated with reasonable certainty that the use of NTA in detergents would not result in significantly detrimental environmental consequences, provided the environmental concentrations resulting from the use of NTA in the U.S. do not exceed the limits reported in studies from usage in Canada. The singular, most important area which should be addressed in order to more fully understand the potential for NTA to cause undesirable environmental effects is related to the study of chronic exposure of mixed communities under realistic environmental conditions. This could be specifically addressed through detailed environmental monitoring.

The use of NTA as a detergent builder assures that it will be released into a variety of aquatic environments through wastewater discharges. Its principal environmental effects, if any, would therefore involve primarily aquatic organisms. NTA has been tested for possible toxicity against a variety of aquatic organisms including algae, invertebrates and fish. NTA has been demonstrated to be generally non-toxic to all organisms tested, except at concentrations greatly exceeding those expected to occur in the aquatic environment as a result of its use in detergents. Two items should be noted: 1) the biological activity of NTA varies according to the characteristics of the aquatic environments in which it has been studied; and 2) current estimated environmental concentrations are based upon use experience in Canada and estimates for U.S. consumption which are less than certain (see Chapter III: Environmental Fate and Concentrations for a detailed discussion).

Studies with all types of organisms have demonstrated an inverse relationship between water hardness and toxicity. Generally speaking, the toxicity of NTA is greater in soft water than in salt or hard water.

The following discussions are related to the effects and behavior of NTA as studied under various conditions. A detailed discussion of these issues (environmental effects) is presented in the Task Force Report to the Great Lakes Research Advisory Board of the International Joint Commission entitled the Ecological Effects of Non-Phosphate Detergent Builders: Final Report on NTA, dated December 1978 (Joseph Shapiro, chairman).

Acute Toxicity

The acute toxicity of NTA is generally in excess of 100 mg/l for freshwater fish and invertebrates. Marine organisms tolerate at least a 10 fold greater concentration of NTA. Rainbow trout and the amphipod

Gammarus pseudolimnaeus appear to be the most sensitive of the species tested, each having a 96-hour LC50 of 98 mg/l in soft water. Refer to Table 8 for a listing of acute toxicity values to freshwater organisms. Mixing quantities of NTA in excess of 100 mg/l in test water, raises the alkalinity of the solution (Arthur et al. 1974) and may also raise pH, especially in soft waters (the pH of a 1% aqueous solution of NTA is 11). This is supported by observations by several investigators (Arthur et al. 1974; Flannagan 1971; Sprague 1968) who attributed at least some of the observed mortality in their studies with NTA to high pH stress. Arthur et al. (1974) demonstrated an increase in the static LC50 for fathead minnows from 255 to 470 mg/l by adjusting the pH of the test solution to 7.7. Biesinger et al. (1974) reported an excellent correlation ($r=0.95$) between total hardness and the LC50 to Daphnia magna during a 3 week exposure. The toxicity in Lake Superior water, with a total hardness of 45 mg/l as CaCO_3 (i.e. soft) was reduced 4.5 fold when hardness was artificially increased to 200 mg/l (CaCO_3).

A similar situation exists for saltwater organisms (refer to table 9). Eisler et al. (1972) found greater toxicity to the mummichog at 15‰/oo, than at 25‰/oo salinity. Tarzwell (1970) demonstrated a 4 fold reduction in toxicity for the marine zooplankter Acartia clausi, which showed a 24-hour LC50 of 550 mg/l at 15‰/oo, but was 2100 mg/l at 30‰/oo salinity.

These reported LC50 values are much greater than the concentration of NTA likely to be found in receiving waters. For example, Brownridge (1977) reported a mean concentration of 0.046 mg/l NTA-Na below sewage plant effluents in areas using detergent formulations with a weighted average of 15% NTA. The maximum measured concentration of NTA in raw wastewater was 22.9 mg/l. Assuming that up to 30% NTA would be used in detergent formulations, the greatest expected NTA concentrations in untreated wastewater would be approximately 40 mg/l. As indicated in the previous chapter (III), biodegradation, photochemical decomposition, dilution and dispersion all combine to make the accumulation and availability of NTA in receiving streams unlikely and levels should be well below the acute toxicity values.

Chronic Toxicity

Chronic bioassays extending over one or more generations have been performed on only a few freshwater fish and invertebrates. Environmental concentrations to which aquatic organisms would likely be exposed are believed to be generally very low due to dilution and degradation (see Chap. III). The Canadian monitoring studies confirm

ACUTE TOXICITY OF WTA-86 TO FRESHWATER ORGANISMS

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Species	Effect Measured	MTA-86 Effect Level	Hardness as mg/l CaCO ₃	Reference
<i>Bosmina corei</i>	96-hr LC50	98	35	Macek & Sturm 1973
<i>Salmo gairdneri</i>				
<i>Fathead minnow</i>	96-hr LC50	127	35	Macek & Sturm 1973
<i>Pimephales promelas</i>				Arthur et al. 1974
<i>Fathead minnow</i>	96-hr LC50	114	ca. 45	Macek & Sturm 1973
<i>Fathead minnow</i>	28 d survival	>96<173	35	Wagner, 1970 Wagner, 1970
<i>Pimephales promelas</i>	96-hr LC50	252	60	Arthur et al. 1974
<i>Bluegill sunfish</i>	96-hr LC50	483	170	Macek & Sturm 1973
<i>Bluegill sunfish</i>	28 d survival	>96<173	35	Wagner, 1970 Wagner, 1970
<i>Snail</i>	96-hr LC50	373	60	Arthur et al. 1974
<i>Pyxis heterostrophus</i>	96-hr LC50	322	170	Flannagan, 1971
<i>Amphipod</i>	96-hr survival	98	ca. 45	Flannagan, 1971
<i>Amphipod spp.</i>	96-hr survival	>500	?	Flannagan, 1971
<i>Gastropod spp.</i>	96-hr survival	>500	?	Flannagan, 1971
11 insect spp. including midges, caddisfly, stonefly, mayfly, dragonfly	96-hr survival	>500	?	Flannagan, 1971
<i>Snail</i>	96-hr survival	>100	?	Flannagan, 1974
<i>Helicoma trivolvis</i>				

Source: Task Force Report, 1978.

TABLE 9

ACUTE TOXICITY OF NTA-Na TO MARINE ORGANISMS

<u>Species</u>	<u>Effects Measured</u>	<u>NTA-Na Effect Level</u>	<u>Reference</u>
Scup, <u>Stenotomus chrysops</u>	168-hr LC50	2200	Eisler et al. 1972
Mummichog, <u>Fundulus heteroclitus</u>	168-hr LC50	5500	Eisler et al. 1972
Striped bass, <u>Morone saxatilis</u>	168-hr LC50	5500	Eisler et al. 1972
Crass shrimp, <u>Palaemonetes vulgaris</u>	168-hr LC50	1800	Eisler et al. 1972
Quahog clam, <u>Mercenaria mercenaria</u>	168-hr LC50	>10,000	Eisler et al. 1972
Hermit crab, <u>Pagurus longicarpus</u>	168-hr LC50	1875	Eisler et al. 1972
Starfish, <u>Asterias forbesi</u>	168-hr LC50	3000	Eisler et al. 1972
American lobster, <u>Homarus americanus</u>	168-hr LC50	3150	Eisler et al. 1972
Bay mussel, <u>Mytilus edulis</u>	168-hr LC50	3400	Eisler et al. 1972
Eastern mud snail, <u>Nassarius obsoletus</u>	168-hr LC50	5100	Eisler et al. 1972
Sand worm, <u>Nereis virens</u>	168-hr LC50	5500	Eisler et al. 1972
Zooplankton:			
<u>Tisbe furcata</u>	72-hr LC50	270	Tarzwel, 1970
<u>Pseudodiaptomus coronatus</u>	72-hr LC50	700	Tarzwel, 1970
<u>Acartia clausi</u>	72-hr LC50	1350	Tarzwel, 1970
<u>Eurytemora affinis</u>	72-hr LC50	1250	Tarzwel, 1970
Crab zoea	72-hr LC50	1650	Tarzwel, 1970
<u>Tigriopus japonicus</u>	72-hr LC50	3200	Tarzwel, 1970

Source: Task Force Report, 1978.

this. The Harbor at Hamilton, Ontario, and the western portion of Lake Ontario have been monitored for NTA regularly since 1971. Most locations in western Lake Ontario have shown NTA concentrations of less than 0.2 ug/l, with a single high value of 162 ug/l in one sample taken near Toronto. Hamilton Harbor results indicated detectable concentrations of NTA at a number of stations, with a high of 94 ug/l. Uncertainty exists for reasons contributing to localized elevated NTA concentrations; contributing factors have been listed as circulation patterns, wastewater outfalls and changing wind conditions. In addition, Canadian monitoring studies have been plagued with uncertainties about sample preparation, differences in analytical methods and a lack of replicate sampling (see Chap. III).

Shannon *et al.* (1974) reported downstream NTA concentrations following discharge from a sewage treatment plant. During warmer temperatures (10°C) in which 95% of NTA was removed in sewage treatment, downstream concentrations were reported to be 10 ug/l. At colder temperatures (.5-3.0°C) following only 5% NTA removal, concentrations were reportedly 106 ug/l.

Monitoring data reported by Prakash (1976) indicated no detectable levels of NTA in the estuarine environments of Vancouver, B.C. or Halifax Harbor, Nova Scotia. As indicated in Chapter III, exact environmental concentrations for the U.S. cannot be positively stated due to differing environmental circumstances and denser populations and subsequent loadings.

The maximum no-effect levels for the species of fish and invertebrates tested exceed the expected environmental concentrations of NTA, with one exception. This singular low level effect was detected from a histopathological study, rather than through a gross observation. Eisler (1972) reported significant intestinal lesions in the mummichog at NTA levels as low as 1 mg/l following exposure for 168 hours. All mummichogs subjected to NTA levels of 10 mg/l or higher exhibited lesions of the ileum and rectum. The incidence of lesions in mummichogs exposed to 1 mg/l dropped to 60% while control groups were reported lesion free. Eisler concluded that NTA might present a significant hazard to marine teleosts and higher invertebrates when used as a partial replacement for sodium tripolyphosphate in household detergents.

Generally, however, the available literature describes no significant adverse effects at low exposure levels.

Arthur *et al.* (1974) reported no observable differences in survival, spawning activity, or egg hatchability of fathead minnows under continuous NTA exposure at 54 ppm for 36 weeks in a chronic (generation-cycle) test. Macek

and Sturn (1973) reported similar results in a study on survival and gill condition in bluegill sunfish and fathead minnows exposed to NTA for 28 days. No gill pathology or significant cumulative toxicity was reported to be induced by NTA exposure up to 96 mg/l during the 28 day period.

Amphipods, Gammarus pseudolimnaeus, were slightly more sensitive, showing reduced survival and reproduction above 19 mg/l (Arthur et al. 1974). It should be noted that the fathead minnows and amphipod study by Arthur et al. (1974) were conducted in soft water and at near neutral pH.

Flannagan (1974) reported decreased adult growth and fecundity above 25 mg/l for the snail Helisoma trivolis. The reduction was greatest, however, in the first generation of this 4 generation study.

Biesinger et al. (1974) reported a 16% reduction in Daphnia magna fecundity at an NTA concentration of 91 mg/l (3 weeks exposure in soft water).

The most resistant of the invertebrates tested was the midge, Chironomus tentans, which showed no ill-effects at 3000 mg/l (Flannagan 1971).

Overall, the chronic toxicity data do not trigger a concern for significant adverse effects. The significance and the cause of the intestinal lesions in Eisler's study with the mummichog are unknown. It is possible that the mummichog is extremely sensitive to NTA, or that it may react similarly to various pollutants. It does appear to be quite tolerant of NTA, with 96 and 168-hour TL50 values reported by Eisler et al. (1972) to be 5500 mg/l. Since this is the most serious effect produced with low levels of NTA reported in the literature it would be highly desirable to repeat the work by Eisler with the mummichog to ascertain if the results are reproducible.

Metals Toxicity

NTA is a strong chelating agent, and it is for this purpose that NTA is incorporated into detergents as a builder. The metal complexing ability of NTA has been one of the most significant factors of environmental concern. As indicated in Chapter III, there are conflicting reports concerning the biodegradation of NTA metal complexes. Metal complexes are of concern because of direct toxicity to aquatic life, as well as sublethal effects resulting from increased metal uptake, to possible eutrophication with algae (refer to "Effects on Algae" for a discussion of this latter effect).

Regarding NTA's ability to chelate metals, Epstein (1970) suggested that poorly degraded NTA chelates could be formed; presenting a readily available source of metals that could conceivably be taken up by and toxic to various aquatic organisms. However, this does not appear to be a significant concern. In fact, several investigators have demonstrated a marked decrease in the toxicity to several organisms by heavy metals when chelated by NTA (Sunda *et al.* 1974; Eisler *et al.* 1972; Gudernatsch 1970; Sprague 1968).

In a series of static and flow-through tests Barica *et al.* (1973) exposed chironomids, crayfish, and rainbow trout to clean and metal supplemented sediments. When NTA was added at 0.2-5 mg/l, the Fe, Mn, Pb and Zn concentrations in water increased slightly. However, the NTA had no significant effect on metal uptake by the organisms. Of all the metals tested, only Mn showed a slight increase in trout tissue after eight weeks.

Epstein (1972) observed in studies with rats that NTA chelated zinc was cumulatively and persistently taken up by bone, particularly in periods of active growth. It should be noted that this and subsequent adverse toxicological observations were produced at concentrations in excess of anticipated environmental levels. In addition, no adverse effects in bone (e.g. decreased strength) were observed. The possibility of chelated metals being absorbed by aquatic organisms (e.g. fish skeletons) and subsequent magnification in food chains or effects on behavior have not been studied extensively, but such effects do not appear likely.

In view of the toxicological effects and uptake of NTA-metal complexes as reported for the various species tested, in combination with the negligible metal mobilization reported from Canadian monitoring programs (Brownridge 1977; Matheson 1977), the question of metals toxicity does not appear to be a serious concern.

Effects on Algae

The results of studies with algae can perhaps be summarized best by Prakash (1976) who pointed out that studies on the effect of NTA on metabolism and growth of planktonic algae in freshwater and the marine environment have been anything but consistent, demonstrating both growth inhibition or growth stimulation, depending upon the species tested and the water characteristics. The available literature indicates that NTA might affect algae growth by three major routes: 1) by perhaps supplementing direct nitrogen requirements of phytoplankton upon degradation, especially in nitrogen limited waters (i.e. estuaries, coastal waters and

oligotrophic lakes); 2) through chelation NTA may increase the availability of other necessary and perhaps limiting trace elements; and 3) by reducing the availability of metals like copper through chelation which normally may be present at near toxic levels to algae. It appears that the variability in the results reported for NTA on algae derives from the variability of the systems in which it was tested. Different aquatic systems vary in their trace metal content and in their community structure. The results of laboratory tests are difficult to extrapolate to natural aquatic ecosystems which consist of various trophic levels and complex interactions and competitions. A milieu of positive and negative influences are at work in natural ecosystems, and the effects of introducing a new factor into these complex relationships depend upon the specific circumstances at the specific moment it is introduced.

Many different approaches have been taken to determine the effects of NTA on algae in order to predict the consequences of its use in detergents. NTA has been tested at low concentrations, at high concentrations, alone, in the presence of sewage wastes, against single species in synthetic media, in filtered lake water, in microcosms, in small enclosures, in large enclosures and for long and short periods of time. A variety of criteria have been used to measure results, ranging from numbers of algae, through carbon-14 fixation rates to species diversity. It is not the purpose of this brief review to discuss the various possibilities for variation in test systems and results. Rather, the tests and their respective results should be considered for relevance to the proposed use of NTA in detergents. Generally, studies using high NTA concentrations, artificial media, single species of algae or short observation periods are interesting, but are not directly applicable. Such studies provide indications of possible effects but do not predict what will happen in various aquatic environments under normal conditions of use. As such, the Canadian experience and monitoring data provide the most relevant information. The Canadian experience as monitored by Proctor and Gamble (Brownridge 1977) reportedly showed that 6% industry wide average NTA content in detergents resulted in a median concentration of 1.7 mg/l of NTA in wastewater, with a maximum of 11.0 mg/l; and that 15% average NTA content in detergents resulted in a median value of 3.6 mg/l NTA with a maximum of 22.9 mg/l. If the greatest amount likely to be present in detergent is about 30% NTA, then the median wastewater influent would likely be about 6 mg/l with a maximum concentration of about 40 mg/l. At these high estimates, the worst case scenario would put the nitrogen contribution by NTA, assuming complete degradation, at a maximum of 2 mg N/l with a median value of about 0.3 mg

N/1 (Task Force Report to the IJC, 1978). This same report states that the inorganic nitrogen content of wastewater effluents is generally in the range of 30-40 mg/l. Therefore, on this basis, the maximum increase in nitrogen would be 5.0-6.6%, with a median increase of 0.75 to 1%. It should be noted that many lakes presently described as nitrogen-limited receive high loadings of phosphorus. Reduction of phosphorus would mean that such water systems would no longer be controlled by nitrogen (as a limiting factor). Generally, it would appear that the overall contribution of nitrogen from NTA is of a magnitude that should result in an insignificant eutrophication effect. Additionally, the literature does not trigger a substantial concern relative to stimulation or inhibition of algae through metals chelation (studies germane to increasing trace metal availability or removing inhibitory levels of toxic metals).

Additional Research

Based upon the low levels detected in the monitoring of NTA during its usage in Canada, significant adverse environmental effects are not anticipated. However, as indicated above, NTA has exhibited both stimulation and inhibition in various algal studies, and its mode of action under actual environmental conditions is still uncertain, indicating that additional research is appropriate. Canadian monitoring has only attempted to determine the presence (or absence) of NTA, and has not investigated effects or impacts, such as possible subtle shifts in algal populations or productivity. Detailed environmental monitoring for such effects is appropriate.

The studies discussed in this review do not provide positive indications that NTA would (or would not) produce environmental hazards; rather, they tend to point out areas of concern where further study is warranted or desirable. The majority of studies which reported adverse effects associated with NTA concentrations do not realistically represent expected environmental levels. While no adverse environmental effects are anticipated, there exist certain information voids and inconsistencies in the available literature (as indicated below) which prevent an absolute and firm conclusion of NTA's environmental safety.

One area of concern is related to the conflicting results reported in several dose-response studies (with fish) with respect to biodegradation of NTA and the actual concentrations of NTA in the test solutions.

Biesinger et al. (1974) performed chronic studies with *Daphnia magna* and reported that analytical measurements for NTA from the test containers were made at the time of

addition and 1 week later. Concentrations of NTA were reported slightly higher a week after addition because of a small amount of water evaporation; no degradation of NTA was evident during the test duration.

Contrary to this observation, Arthur *et al.* (1974) in their study of the toxicity of NTA to the fathead minnow and an amphipod reported that biodegradation of NTA was observed during both the fathead minnow and amphipod chronic tests. The concentrations of NTA in the stock bottles were maintained through addition of fresh NTA solution to replace that which was lost due to degradation.

It is possible that these conflicting observations are normal and could be reproduced. Still, they raise the question of whether or not biodegradation occurs and is evaluated in typical toxicity studies to insure that the desired test concentration is maintained throughout the test. Since degradation occurs in some test solutions, results of studies where analysis for NTA was not performed could be less than accurate. For example, the major study of the toxicity of NTA to marine macroinvertebrates and fish (Eisler *et al.* 1972) did not check for NTA degradation. Biodegradation in Eisler's test would affect the validity of his results, particularly since he conducted the tests for up to 168 hours.

A final factor related to NTA's possible adverse effects on fish and other aquatic organisms is the apparent lack of degradation in estuarine systems, as reported by Bourquin and Przybyszewski (1977) and by Gledhill and McDonald (1976). Both the reasons for the apparent lack of degradation and the potential effects of NTA persistence are currently unknown. The LJC Task Force Report (1978) noted that: "...because of the versatility of microorganisms (in estuarine systems), it is likely that NTA will not remain in such systems. Further study is required however." NTA's possible effects on saltwater algae and its effects on other estuarine organisms, such as the shell forming mollusks, should be investigated. Also desirable are additional studies involving chronic exposure of mixed communities to low levels of NTA to determine NTA's possible effects on behavior, physiology, histopathology and cytopathology of aquatic organisms.

In any case, analysis for determination of actual versus nominal NTA concentrations should be conducted during all bioassays with any species. In addition, confusion surrounding the interpretation of test results could be avoided by also controlling pH, alkalinity, hardness, and chelate concentration independently.

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APPENDIX A

Conclusions of Selected NTA Review Committees

1. Assessment of the Potential of Nitrilotriacetic Acid to Compromise Human Health. Final Report of the Assistant Secretary of Health, Education and Welfare's Ad Hoc Scientific Group on NTA. 1972. Lauren A. Woods, Chairman.

The Woods Committee concluded that the NTA is a reasonably safe compound under acute or short term exposure conditions. Long term, low level exposure hazards to human health could not be evaluated at that time from the available experimental data. Histopathologic changes associated with NTA were limited to only one organ, the kidney. However, an increase in nonspecific renal changes was associated with the lowest dose of NTA which was administered over a long time period.

"NTA is readily absorbed from the gastrointestinal tract of the rat and dog, but poorly absorbed from the tract of the rabbit, monkey, and man. The major routes of excretion following oral ingestion are via urine and feces. NTA has not been demonstrated to be significantly biodegraded in any mammalian species studied.

"Unpublished studies using submammalian tests fail to show any increase in point (gene) mutation due to NTA. The tests that respond to chromosomal changes are conflicting. It seems possible that NTA, under some experimental circumstances, might adversely affect chromosome integrity.

"A review of available teratogenic studies indicated that there was no increase in congenital defects in the fetuses exposed experimentally to NTA as compared to controls.

"A survey of literature failed to reveal any long-term studies designed for detection of the potential carcinogenicity of NTA. Other long-term studies were inadequate for this purpose."

The committee recommended that "if use of NTA is permitted in detergents, the content of NTA in detergents should be printed on the package, and the following parameters be continually monitored with a reappraisal after 3 years:

1. Levels of NTA in ground and surface waters.
2. Levels of nitrogen in ground and surface waters.
3. Levels of NTA in fresh-water fish and fish-eating birds.
4. Levels of NTA in human bone.
5. Levels of zinc in human bone.
6. Incidence of human degenerative renal disease.
7. Epidemiologic studies of any special populations subjected to heavy exposure of NTA with special attention to the most sensitive members of the population as indicated by age and health."

Finally, the Committee considered that "the condition of man's environment is also vital to any consideration of his well being. For this reason, the committee believed that the role of NTA as a possible agent for reducing eutrophication must be considered in addition to consideration of the possible direct role of NTA upon the human body."

2. International Joint Commission Task Force on the Health Implications of NTA. 1977. Paul D. Foley, Chairman.

The task force "accepted the conclusions expressed by 'The Woods Report,' and reviewed and accepted additional studies on potential mutagenic effects of NTA which are essentially negative." The committee concluded that:

"NTA single dose acute and subacute toxicities are very low and compatible to that of Sodium Tri-polyphosphate (STP) which it would replace in detergent formulations.

"Three new carcinogenicity studies were reviewed in detail. In the studies, sodium NTA was fed to rats at doses from 200 to 20,000 ppm in diet and sodium NTA and acid form NTA to rats and mice at 5,000, 7,500 and 15,000 ppm in diet. One study fed acid NTA at 1,000 ppm in drinking water to rats.

"A statistically significant effect was observed for tumors of the kidney and/or urinary tract in all studies. There was also an observed increase in liver cancer although the occurrence was only sporadic.

"The ten-fold increase in urinary elimination of zinc recorded in all experiments administering large doses of NTA was considered significant but its etiologic significance towards the production of tumors of the urinary system has not been established. One can only speculate that a sensitive balance has been upset by

the loss of zinc without similar losses of cadmium and other trace elements. It is concluded that the principal human exposure to NTA is by drinking water. The Progress Report on the Canadian Monitoring Program puts public water supply levels at 10 ppb with an occasional maximum of 50 ppb; 96% of all samples contained less than 25 ppb.

"The assessment of carcinogenic risk to humans from present levels of NTA in the environment was considered extremely tenuous. The extrapolation from high dose in animals to low dose in humans must be done on a most conservative basis. To assess the potential risk to man, the difference in absorption of NTA in man and rodents must also be considered."

3. International Joint Commission Task Force on the Ecological Effects of Nonphosphate Detergent Builders - NTA 1973. Joseph Shapiro, Chairman.

"The Task Force concludes that the extensive literature and Canadian experience indicates that the use of NTA does not constitute an obvious environmental hazard, however, a number of important questions remain. The Task Force feels that more work should be done to resolve these questions.

"Based on this conclusion, the Task Force recommends that NTA should not be prohibited from use as a detergent builder. The Task Force further recommends that its use be accompanied by studies to address the following questions:

- (1) "Under aerobic biological wastewater treatment regimes and in most circumstances in fresh water systems NTA ordinarily degrades rapidly. However, the Canadian monitoring experience did reveal that low concentrations of NTA may be found in the aquatic environment. The task force feels that the forms in which NTA exists at these low concentrations should be investigated.

"Whenever any new organic compound is released to the environment, there is concern over its persistence. By recommending that the persistence of NTA be investigated, we are in no way comparing the properties of NTA to such materials as halogenated hydrocarbons. On the contrary, we recognize the clear difference between NTA and such substances. But from the Canadian experience, NTA does appear to persist at low levels and it is important to know whether this is because of the kinetics of microbial activity, or because of the

presence of nondegradable correlates. For example, low temperatures slow the degradation of NTA preferentially and the acclimation time to attain NTA degradation is greater than more readily biodegradable wastewater constituents.---

- (2) "Although NTA degrades rapidly in most aerobic environments, studies on its ability to degrade during anaerobic waste treatment or under anaerobic environmental conditions are inconclusive. The task force feels that the question needs further study.---

"Some controversy exists on the ability of NTA to degrade under "anaerobic conditions." Some of this controversy may rest on the question of whether certain systems were indeed anaerobic, but in other cases anaerobic degradation apparently has occurred. Furthermore, it has occurred where the concentration of nitrate was probably too low to serve as an electron acceptor. The situation requires clarification.---

- (3) "No investigations have been conducted to determine the concentrations of NTA in anaerobically digested sludges. Canadian studies have shown that about one-third of the NTA appears to be lost from solution during primary treatment. Because it may be settled out in the sludge and because sludge is frequently deposited in the sea and on land, investigation is necessary.

"Because anaerobic degradation of NTA remains in question, it cannot be counted on and therefore it is likely to show up in sludges where some, but not necessarily all, will be degraded aerobically. The extent to which it thus persists and comes in contact with land plants and aquatic organisms needs study.

- (4) "Although NTA does degrade in aerobic waste treatment the Task force feels that its behavior in physical-chemical treatment processes needs elucidation.

"Little if any information is available on the removal of NTA by such processes as alum coagulation, lime coagulation, iron coagulation, carbon adsorption, etc. Although such processes are likely to follow aerobic wastewater treatment, their effects on NTA should be known.

- (5) "NTA degradation has been studied at intermediate pH values [3-9] and at temperatures in the low to moderate range. The behavior of NTA at low and

high environmental pH values and at temperatures expected in thermophilic waste treatment processes should be evaluated.

"Many eutrophic softwater lakes, particularly those receiving wastewater effluents, maintain pH values well in excess of 9 for long periods of time. Similarly, an increasingly large number of streams and lakes is developing low pH values, below 5, not only from acid mine drainage in areas such as West Virginia, but in the northeast United States, as well as in southern Scandinavia, from acid rain.

- (6) "Degradation of WTA in marine and estuarine systems appears to be very slow. The Task Force feels that because of the versatility of microorganisms it is likely that WTA will not remain in such systems. Further study is required, however.

"Degradation of WTA by marine organisms has been demonstrated, but in estuarine systems there apparently is inhibition of the degradation by freshwater organisms. The possibility of accumulation of WTA in such systems should be further examined.

- (7) "WTA does not solubilize and transport heavy metals to an appreciable extent under most circumstances. However, the Task Force feels that its behavior in systems of high inorganic turbidity and/or high metal content needs investigation.

"There are specific systems where reaction of WTA with heavy metals and subsequent transport of the metals might be especially important. Among these are waters receiving drainage from mining operations. Such systems have not been examined.

- (8) "Available information indicates that acute toxicity to aquatic organisms resulting from environmental concentrations of WTA is unlikely. Similar studies on chronic toxicity suggest the same. Elucidation of the mode of toxicity would allow a better evaluation of the likelihood of chronic toxicity to organisms not specifically tested under various environmental conditions.

"It is evident that not all aquatic organisms can be tested for their susceptibility to WTA. Similarly, all the environmental conditions cannot be tested. Thus, it is important to develop principles to assist in prediction of toxicity, chronic or

acute, but especially the former. Without such information, we are forced to rely on empirical observations.

- (9) "NTA is not expected to increase eutrophication by providing nutrients from its decomposition. Furthermore, most experiments with simple systems indicate that it does not stimulate algal growth. However, the long term studies using whole ecosystems have not been performed to the extent of satisfying the Task Force that NTA will not cause significant changes in aquatic community structure. Such experiments are necessary.

"One of the least satisfying aspects of the testing of detergent builders has been that on the aquatic community. Too often studies have been done using single species of algae, and when community studies were done they were either unrealistic, too short, insufficiently studied, or omitted important aspects of the community. Studies of the results to date do not raise any specters, but the final answer is not yet in."

6. National Toxicology Program. Subcommittee Report. Review of Procter and Gamble Statement Regarding Carcinogenesis of NTA. January 1980.

The NTP subcommittee addressed specific statements submitted to it by the Procter and Gamble Company. The Statements and Subcommittee findings are summarized below.

A. Procter and Gamble Statements

"The Procter and Gamble statements propose that NTA is an indirect or secondary carcinogen and does not produce any adverse health effect to people at exposure levels present in water associated with widespread use of household detergents because

NTA is not a mutagen;

renal cell tumors are preceded by morphological evidence of vacuologensis which is dose related (threshold) and is reversible; and,

the mechanism for induction of tumors in rats fed NTA at high doses is related to crystalluria and changes in cations in renal tubular cells, particularly calcium and zinc.

B. Subcommittee Conclusions of Review of Procter and Gamble Data and Other Relevant Evidence

"The Subcommittee concludes from its review that there is no evidence that NTA is a mutagen; and, NTA is a renal urinary tract carcinogen in rodents. There may be a threshold for vacuologenesi but the relationship of this morphologic feature and neoplasia has not been demonstrated. There is also no evidence that reversal of morphologic effects on kidneys following termination of exposure has any effect on tumor formation. The relationship of changes in calcium and zinc content of kidney cells to carcinogenesis has not been demonstrated. Therefore, we do not know the mechanism of NTA carcinogenesis and do not know what level of exposure constitutes a threshold, if there is a threshold."

C. Subcommittee Estimates of Human Exposure and Assessment of Risk from Rodent Data

Risk from Drinking Water

"Drinking water supplies in Canada were found to contain an average of 2.8 ppb resulting in an average exposure of 0.07 ug NTA/KG/day. Several studies have shown an increase in urinary tract tumors in both sexes of mice and rats at high dosages. Using linear extrapolation the maximum potential urinary tract tumor risk in rodents at the average drinking water exposure level (0.07 ug/kg/day) is estimated to be less than 2×10^{-7} ."



THE PROCTER & GAMBLE COMPANY

OFFICE TECHNICAL CENTER

June 25, 1979

CINCINNATI, OHIO 45217

Dr. Wayne Galbraith
Health Review Division (TS-792)
Office of Toxic Substances
U.S. EPA
401 M Street S.W.
Washington, D.C. 20460

Dear Dr. Galbraith:

This letter is to follow-up our June 13 phone conversation relative to my June 4 letter to you concerning Procter & Gamble's inhalation toxicity testing with NTA. In an effort to respond as rapidly as possible in providing information concerning Procter & Gamble's inhalation testing as you requested during our May 31 phone conversation, I had to use what information was available to me, namely a several year old summary of our inhalation testing, which formed the basis of my June 4 letter. On June 13, I called to indicate that we had retrieved the entire report from storage, that one of our toxicologists had reviewed the report, and that his review had uncovered some transcription errors between the summary and the report. The purpose of this letter, then, is to correct the transcription errors, as you suggested during our June 13 phone conversation. In addition, the wording in certain locations of my June 4 letter is modified and some further discussion is included to provide additional useful information. Importantly, these changes do not affect the findings that NTA was less irritating to the respiratory tract and less toxic than sodium tripolyphosphate.

The format chosen to present the changes is one of reproducing here the exact wording of the inhalation toxicity section of my June 4 letter (section 1). Words to be changed are lined out with dashes (----), and the corrections/ additional wording follows and is underlined(____). Quote, from my June 4 letter:

"1. Inhalation Toxicity. Inhalation toxicity studies have been conducted with NTA and with sodium tripolyphosphate (STP) for comparative purposes. In net, the results show NTA to be less irritating to the respiratory tract and less toxic than STP. This conclusion is drawn from the results of the following tests:

- * Pulmonary Irritant Screening - mice
- * Inhalation LC₅₀ - rats
- * 4-Day Repeated Exposure - rats
- * 4-Week Repeated Exposure - rats, guinea pigs, monkeys

A. Pulmonary Irritant Screening.

In this test, mice were exposed for 5 minutes to aerosols containing four different levels of NTA ranging in concentration from 200-7500-ppm.

220-7600 $\mu\text{g/l}$ or to four levels of STP ranging in concentration from 200-3250 $\mu\text{g/l}$. The mice were secured in a plexiglas cylinder and connected to a polygraph which measured respiration rate, depth of respiration and gave a respiratory pattern. These were compared with data from control animals the control period and a qualitative measure of respiratory irritation defined as slight, moderate or severe was then developed for the test materials. Under the conditions of this test NTA was classed as a slight to moderate respiratory irritant over the range of 200-1410 $\mu\text{g/l}$ and as a severe irritant at 7600 $\mu\text{g/l}$; slight sensory irritant at 220 $\mu\text{g/l}$, a moderate irritant at 1090 and 1410 $\mu\text{g/l}$, and a severe irritant at 7600 $\mu\text{g/l}$. STP was a slight to moderate respiratory irritant over the 200-300 $\mu\text{g/l}$; 200-380 $\mu\text{g/l}$ range and a severe irritant at 2120 and 3250 $\mu\text{g/l}$.

B. Inhalation LC₅₀.

Ten male albino rats at each dose level were exposed for 4 hours to: (1) non-micronized NTA at levels of 3.3, 3.6, and 5.0 mg/l and to non-micronized STP at levels of 2.6, 3.0, and 4.5 mg/l; and (2) micronized NTA at 5.0 mg/l, STP at 4.5 mg/l and a 1:1 mixture of NTA/STP at 5.5 mg/l.* Survivors were observed for 14 days, then necropsied. No mortalities were observed at any of these exposure levels. Observations made on exposed animals included salivation, slow labored respiration, partially closed eyes and hypoactivity. All animals recovered after 1-2 days the exposure and appeared normal and healthy during the remainder of the 2 week observation period. Body weights at 15 days were normal for all test groups and necropsies of treated animals revealed no differences consistent differences from the controls. The highest concentration in each instance was the maximum level attainable under dynamic exposure conditions utilizing a cyclone dust generator or a pulse-puff generator.

The LC₅₀'s determined in this test are thus as follows:

	LC ₅₀ (mg/l)
NTA	>5.0
STP	>4.5
NTA/STP (1:1)	>5.5

C. 4-Day Repeated Exposure.

This study employed 10 male albino rats at each dose level. The animals were exposed to micronized materials 6 hours/day for 4 days followed by a 14 day observation period and were then necropsied. The exposure levels and observed mortalities were as follows:

*These were measured concentrations.

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Calculated Desired
Concentration
mg/l

Air Controls
0.002
0.02
0.2
2.0

NTA	Mortalities		NTA/STP (1:1)
	STP		
0/16 10	0/16 10	0/16 10	
0/16 10	0/16 10	0/16 10	All 15's
0/16 10	0/16 10	0/16 10	should
0/16 10	0/16 10	0/16 10	be 10's
0/16 10	3/16 10	0/16 10	

No pharmacotoxic signs were observed in the three low dose levels, with the exception that rats exposed to 0.2 mg/l of STP showed salivation (5/10), coughing (10/10), labored breathing (2/10) and signs of eye irritation (5/10) at day 2-4 of exposure. At the highest dose level all animals showed pharmacotoxic signs indicative of respiratory, nasal and eye irritation; the high dose level of STP elicited three deaths (one during treatment; two post-treatment) and the survivors exhibited coughing, gasping, hypoactivity, salivation and debilitation. After 14 days of observation the NTA-treated animals in all dose groups appeared normal. The NTA/STP-treated animals in all test groups except the highest level also appeared normal. The high level group exhibited an opaque film over the eyes. The STP-treated animals in all but the high dose group appeared normal after 14 days. The surviving animals in the high dose group remained in a debilitated state with labored respiration and red crusts around the eyes throughout the 14-day observation period. Gross observations at necropsy revealed no treatment-related abnormalities. In general, these three test materials exhibited a low order of toxicity when exposed to rats by inhalation for four consecutive days.

D. 4-Week Repeated Exposure.

The test protocol incorporated three exposure levels (plus controls) of non-micronized NTA, STP, and the 1:1 mixture of NTA/STP with monkeys (4/dose level), rats (12/dose level) and guinea pigs (12/dose level). The animals were exposed 6 hours/day, 5 days/week for 4 weeks followed by a 2 week observation period. The exposure levels were:

Desired (Calculated) Exposure, ug/l	Actual (measured) Exposure, ug/l		
	NTA	STP	NTA/STP
0	0	0	0
10	10	13	11
250	213	137 (150)**	215
500	342	343 (300)**	475

**Calculated exposure.

*Some areas of darkness were observed on the lung surface of rats exposed to the NTA/STP mixture at the three highest levels and sacrificed on the day following the fourth and last exposure. These changes were not observed in rats and were sacrificed at the end of the 14 day observation period.

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For NTA, exposure of rats, guinea pigs and monkeys to 10 and 213 $\mu\text{g}/\text{l}$ failed to elicit any pharmacotoxic response. At the 342 $\mu\text{g}/\text{l}$ level of NTA, some rats (2/12) and guinea pigs (4/12) exhibited dyspnea during the first 2 weeks of exposure; the monkeys exhibited diarrhea but no respiratory irritation or general discomfort. No deaths occurred in any of these animals.

For STP, rats, guinea pigs and monkeys receiving exposure at 13 $\mu\text{g}/\text{l}$ were not adversely affected. Respiratory distress and six deaths were incurred by guinea pigs exposed to 137 $\mu\text{g}/\text{l}$. Rats and monkeys were unaffected at this concentration. Major respiratory distress, in the form of dyspnea, coughing and gasping, was exhibited by guinea pigs exposed to STP at 345 $\mu\text{g}/\text{l}$. ~~Eleven~~ ^{of 12} animals died during the four weeks of exposure. Rats and monkeys exhibited few pharmacotoxic signs.

For the NTA/STP mixture, rats, guinea pigs and monkeys at the various exposure levels did not exhibit any exhibited very minimal or no outward manifestations of discomfort during the entire exposure period or 2 week post-exposure observation period. No apparent compound-related deaths occurred in any of these animals.*

Growth curves from animals exposed to NTA, STP and the NTA/STP mixture were generally comparable to the control or normal growth patterns demonstrated by rats, guinea pigs and monkeys over a six-week period.

Hematological determinations performed on rats and monkeys following the last exposure (day 28) and two weeks thereafter (day 42) did not reveal any abnormalities or trends of effects which were considered to be compound-related.

Biochemical determinations of blood serum from rats exposed to NTA, STP, and the NTA/STP mixture at day 28 revealed increases in SGOT, albumin, globulin, total protein and gamma globulin. With the exception of gamma globulin levels, all other values had returned to the control range by day 42.

Monkeys exposed to these test materials at the same concentrations did not exhibit similar biochemical findings as observed in the rats at day 28. Total protein was elevated in the two lowest dose groups exposed to NTA and in the intermediate dose group exposed to the NTA/STP mixture, and globulin was increased in the two lowest dose groups exposed to the NTA/STP mixture. Increases were also recorded in chloride ion, bilirubin and BUN in all groups exposed to the NTA/STP mixture. With the exception of increased BUN in the highest dose group exposed to the NTA/STP mixture, all other values had returned to the control range by day 42.

*One guinea pig died during the first week of exposure to the low concentration (11 $\mu\text{g}/\text{l}$) and two guinea pigs died during the second week of exposure to the intermediate concentration (125 $\mu\text{g}/\text{l}$). In the absence of dose-response, these deaths do not appear to be compound-related.

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Analyses of trace metals in the urine of rats and monkeys did not reveal consistent abnormal values or trends which could be directly attributed to exposures to any of the test materials.

Pulmonary function studies on monkeys indicated there were no consistent increases or decreases that would imply a trend of effect in various parameters, including total respiratory system flow resistance, N_2 washout, and rate of CO diffusion.

The necropsy findings from rats, guinea pigs, and monkeys which either died during the exposures, or that were sacrificed on days 28 or 42, did not reveal any consistent observations which could be attributed to exposures to any of the test materials." (End of quotation from my June 4 letter.)

This concludes the modifications to my June 4 letter. The other parts of that letter (sections 2 and 3) are not affected. I ask that this letter be attached to and kept with my June 4 letter for purposes of record.

Please feel free to contact me if you have any questions concerning this or any other information relating to your review of NTA. We would be happy to meet with you for any discussions that you believe would be helpful.

Sincerely yours,

THE PROCTER & GAMBLE COMPANY

William D. Hopping

William D. Hopping
Packaged Soap & Detergent Division

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